ALEXION
AstraZeneca Rare Disease

May 22, 2023

William N. Parham, III, Director
Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
Centers for Medicare & Medicaid Services
7500 Security Boulevard Baltimore, Maryland 21244

RE: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

Dear Mr. Parham:

Alexion, AstraZeneca Rare Disease (Alexion) appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS') proposed information collection request (ICR) for the Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA).[1]

Alexion is the group within AstraZeneca focused on rare diseases. Our mission is to transform the lives of people affected by rare diseases through the development and delivery of innovative medicines as well as supportive technologies and health care services. For 30 years, patients and their caregivers have been at the center of everything we do, and our mission is driven by understanding who they are as unique individuals, not just their disease. Every day, we are inspired to think differently and follow the science to create better outcomes for them and their families.

Consistent with our mission, we continue to urge CMS to implement the IRA in a manner that preserves the incentives of the Orphan Drug Act. The express purpose of the ODA is to encourage the development of innovative pharmaceutical products to treat diseases and conditions with very small patient populations, defined by Congress as those affecting fewer than 200,000 persons in the United States. While the IRA includes an orphan drug exclusion, evincing a clear intent to preserve Congress' longstanding support and incentives for drugs treating small patient populations, CMS' approach to implementing this exception fundamentally disrupts this purpose by leaving unprotected rare disease therapies that treat fewer than 200,000 patients in aggregate, thus undermining a carefully crafted framework that has been remarkably successful in bringing new lifesaving treatments to patient populations that may otherwise have lacked access to any treatment for their rare condition.

However, to the extent rare disease therapies become subject to negotiation under the Medicare Drug Price Negotiation Program (the "Negotiation Program"), it is essential that the information CMS collects to effectuate that negotiation fully captures the value of a given rare disease

[1] 88 Fed. Reg. 16,983 (March 21, 2023).

therapy. We have provided general comments regarding the proposed ICR in addition to comments for specific questions in Section H, below.

I. CMS Should Use Certain Core Principles in Assessing the Value of Each Selected Drug.

While Alexion appreciates that CMS is required by statute to take into consideration certain factors in setting the maximum fair price (MFP) for a selected drug, we note that such factors are to be considered only "as applicable to the drug" and not all the statutory negotiation factors must be weighted equally. It is important to ensure there are incentives to develop therapies for all diseases, particularly those for which there are small patient populations, where there is often a weak business case for investment. A model that fails to consider the value of a therapy to patients undermines incentives for innovation in rare disease. We therefore recommend that CMS adopt a framework to both collecting and analyzing data that accounts for the value of a product using the five core principles outlined below, and consider the manufacturer-specific factors only for those therapies that do not represent a therapeutic advance or address an unmet medical need.

Core Principles for Value Assessment. The IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider "evidence about therapeutic alternatives," including comparative effectiveness research, and the extent to which a selected drug represents a therapeutic advance or addresses unmet medical needs. In CMS's initial guidance regarding the Negotiation Program, CMS proposed to first develop a starting point for the initial offer, and then adjust that starting point based on the clinical benefit of the selected drug. As described in our recent comments in response to that guidance, we urge CMS to apply the following five core principles in conducting this assessment:

1) **Transparency:** Using scientific principles, consistent methodology, and appropriate evidence, various stakeholders should be able to come to similar conclusions.
2) **Consideration of contextual factors:** Assessment of rare disease treatments requires special consideration of the study recruitment challenges, lack of disease-specific endpoints, and other factors that shape the evidence which would ultimately inform value assessment.
3) **Selection of appropriate therapeutic alternatives:** Therapeutic alternatives should be based on clinical, not economic factors, and should be limited to FDA-approved treatments within the targeted patient population and line of therapy.
4) **Holistic perspective:** The definition of value should include patient-experience factors, impacts on population health equity, healthcare system resource utilization, and societal impacts outside the healthcare system.
5) **Consideration of a broad spectrum of data sources:** In addition to clinical trial data, value assessments should include data from patient registries and other real-world data sources.

Manufacturer-Specific Factors. The IRA also directs CMS to consider certain "manufacturer-specific data." In the initial guidance, CMS proposed to apply adjustments using these factors as the last step in developing an initial offer. Alexion is concerned with the approach to the collection of these data as outlined in the proposed ICR. For instance, CMS is seeking extensive

information on manufacturer research & development (R&D) costs as well as global recoupment of development costs.

Particularly given the lack of information in the initial guidance regarding the nature and scope of the adjustments CMS intends to make using these manufacturer specific factors, Alexion is concerned that the extent to which manufacturers have recouped their R&D costs will have undue weight on the price of selected drugs. Although obviously very important to drug discovery and development, the amount of R&D costs for a drug are not necessarily indicative of the drug's value. Indeed, while developers may expend large R&D investments to develop a product that ultimately brings tremendous clinical value, products with lower R&D spend can have an equal or greater value. Conversely, products with significant R&D costs may not work any better than the current standard of care, or only marginally better. We therefore recommend that CMS consider the manufacturer-specific factors only for those therapies that do not represent a therapeutic advance or address an unmet medical need.

II. Section H. CMS Should Adopt Rare Disease-Specific Standards to Evaluate Evidence Regarding Alternative Treatments.

As noted above, the IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider "evidence about therapeutic alternatives," including comparative effectiveness research, and the extent to which a selected drug represents a therapeutic advance or addresses unmet medical needs. As CMS develops a benefit assessment framework for selected drugs that are orphan drugs, it must do so with a recognition that rare diseases are rare and heterogenous, and thus tend to be less well understood than more common diseases. CMS should thus adopt special considerations that recognize some of the data and other limitations associated with orphan therapies. Alexion urges CMS to apply the five core principles, described above, in considering these factors. We outline specific recommendations, below, regarding how CMS can apply these five principles to improve the quality, utility, and clarity of the information to be collected for selected drugs that are orphan therapies.

1. Question 41: CMS Should Provide Greater Clarity Regarding the Selection of Therapeutic Alternatives and Consider Both Clinical and Non-Clinical Factors in Assessing Therapeutic Advance.

The IRA requires CMS to consider ''[t]he extent to which [a selected] drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives."[2] CMS proposes to solicit information related to this factor in Question 41 of the proposed ICR. To enhance the quality, utility, and clarity of information collected, we recommend that CMS provide greater clarity regarding the selection of therapeutic alternatives and solicit information to demonstrate whether a selected drug represents a therapeutic advance across a wide range of both clinical and non-clinical factors.

Selection of Therapeutic Alternatives. The instructions for Question 41 ask respondents to "[s]pecify the therapeutic alternative and indication of the selected drug that you are discussing." Alexion supports the collection of information on this issue from the public at large, as the

[2] SSA § 1194(e)(2)(A).

selection of therapeutic alternatives should be a multi-stakeholder process, including the perspectives of patients, clinicians, and manufacturers.

The ICR does not provide a definition of a therapeutic alternative, however. While some flexibility and consideration of contextual factors is necessary in applying the negotiation factors, to enhance the quality and utility of the information considered, CMS should provide some guidance to the public regarding the criteria for the identification of selected therapeutic alternatives.

As outlined in our core principles above, the identification of therapeutic alternatives should be based on clinical, not economic factors, and include only FDA-approved treatments within the targeted patient population and line of therapy. Manufacturers also should be given an opportunity to weigh in regarding CMS's selection of therapeutic alternatives as certain studies have drawn improper comparisons across therapies.

We also note that, in some cases, a selected drug may truly have no therapeutic alternatives. As a leader in rare disease treatment development, we are deeply interested in ensuring that CMS's benefit assessment for selected drugs without therapeutic alternatives is appropriately calibrated to account for the unique characteristics of rare disease and to appropriately recognize the value of orphan drugs. We therefore recommend that CMS solicit information needed to identify those selected drugs for which there exists no appropriate therapeutic alternative. When this is the case, we recommend that the therapy automatically be considered to represent a therapeutic advance and to address an unmet medical need.

Definition of Therapeutic Advance. The concept of therapeutic advance is similarly not specifically defined in the proposed ICR. Consistent with our recommendation that CMS adopt a holistic approach to value assessments we agree that this term should not be specifically defined. However, to enhance the quality, utility, and clarity of information collected, we recommend that CMS solicit information regarding certain specific factors for rare disease therapies, in particular, including: (1) family and caregiver impacts; (2) population health equity; (3) impacts outside of the healthcare system; (4) patients' lived experiences; and (5) consideration of disease prevalence and severity. To illustrate, with respect to patients' lived experiences, considerations such as patient convenience due to route of administration, caregiver burden, and improvements in quality of life not otherwise measured by endpoints in a clinical trial nevertheless represent a significant benefit to the patient. These quality-of-life improvements may seem clinically insignificant, but can directly impact other health outcome metrics, such as medication adherence and patient self-sufficiency. We urge CMS to not only take into account these patient-centric factors, but to prioritize them when assessing the value of a drug product.

Beyond soliciting information from the public regarding these factors, we also recommend that CMS actively include affected patients in the negotiation process to obtain their perspective as to how these factors apply in the real world. Any determination of therapeutic advance or of unmet medical need must explicitly include a framework for weighing the patient and caregiver voice and lived experiences, in addition to clinical factors such as disease prognosis and the lack of alternative therapies. These voices are doubly important in the context of diseases without

therapeutic alternatives, which is often the case for rare disease, as 90 percent of rare diseases currently lack any approved therapy.[3] Unfortunately, the patient voice is often ignored, particularly among people of color with rare diseases, who face additional disparities in access to care, delayed or missed care due to a lack of transportation, and underrepresentation in clinical trials and research.

2. Question 42: CMS Should Collect Real-World Evidence and Adopt an Approach for Comparative Effectiveness Data Specific to Rare Disease.

The IRA also requires CMS to consider "[c]omparative effectiveness of [a selected] drug and therapeutic alternatives to such drug, taking into consideration the effects of such drug and therapeutic alternatives to such drug on specific populations, such as individuals with disabilities, the elderly, the terminally ill, children, and other patient populations."[4] CMS proposes to solicit information related to this factor in Question 42 of the proposed ICR. Alexion supports CMS's consideration of comparative effectiveness in an indication- and population-specific manner, as well as CMS's policy of not considering quality-adjusted life years (QALYs) for purposes of the Negotiation Program, which is consistent with the plain statutory language of the IRA. However, to enhance the quality, utility, and clarity of information collected, we recommend that CMS solicit real world evidence, and adopt an approach for comparative effectiveness data specific to rare disease.

Real-World Data. Alexion supports CMS's view that comparative effectiveness assessments should consider "health outcomes, surrogate endpoints, intermediate outcomes, patient-reported outcomes, and patient experience."[5] However, consistent with the need for the negotiation process to be informed by a broad spectrum of data sources, the data considered to inform comparative effectiveness assessment should include real-world data in addition to clinical trial data.

Unique Approach for Rare Disease. In assessing the effects of a selected drug on specific populations, CMS should collect comparative effectiveness information regarding issues specific to rare disease populations and orphan drugs. While we recognize that the Negotiation Program differs in key respects from international value assessment programs, there are some useful examples that can be drawn from these international programs regarding the unique treatment of rare disease therapies that CMS could apply to the Negotiation Program.[6]

In some cases, these international programs exempt rare disease drugs from the process altogether. For instance, in some countries, orphan drug status and regulatory approval are sufficient to grant reimbursement at a manufacturer specified price with no separate value assessment.

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[3] Austin et al. (2018). Future of Rare Diseases Research 2017–2027: An IRDiRC Perspective. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759721/pdf/CTS-11-21.pdf.
[4] SSA § 1194(e)(2)(C).
[5] Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW) at 41.
[6] *See generally,* Alexion, AstraZeneca Rare Disease, The Innovative Medicines Fund: A catalyst to drive access to rare disease treatments? September 2021, available at: https://alexion.com/Documents/IMF-White-Paper.pdf.

Other countries have created unique HTA programs specifically intended to evaluate treatments for rare and severe diseases with high unmet need. Programs such as these may consider a more holistic perspective of treatment value, including factors such as economic impacts outside of healthcare budgets and benefits to biomedical research and innovation. These programs may also make modifications to the value assessment methods applied to treatments for more common diseases, such as multipliers applied to health benefits to reward treatments for severe diseases, and a willingness to pay higher prices. To the extent rare disease therapies are negotiated, CMS should apply similar considerations as part of the Negotiation Program and ensure the agency is soliciting the information necessary to do so.

3. Question 43: CMS Should Adopt a Broader Definition of Unmet Medical Needs.

The IRA also requires CMS to consider "[t]he extent to which [a selected] drug and therapeutic alternatives to such drug address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy."[7] The proposed ICR provides a definition of unmet medical need as part of Question 43: "A drug or biologic that treats a disease or condition in cases where very limited or no other treatment options exist is considered to meet an unmet medical need." Alexion is concerned that this definition is much too limited.

Consistent with the fourth core principle outlined above, we instead urge CMS to define unmet need in a manner that considers patient-experience factors, impacts on population health equity, healthcare system resource utilization, and societal impacts outside the healthcare system. These considerations are particularly important for rare disease therapies.

To be equitable, any definition of unmet need must consider the unique challenges faced by rare disease patients. While each rare disease affects very few patients, there are thousands of rare diseases. Many of these rare diseases are debilitating and result in a significant amount of suffering for patients, and some of these diseases affect only a very small patient population. For example, atypical hemolytic uremic syndrome is estimated to affect only approximately 900 Americans. It also often takes years for a rare disease patient to be diagnosed, and even once diagnosed, patients face challenges accessing treatment facilities and economic challenges due to difficulty maintaining employment.[8]

Drug development is an exceedingly expensive endeavor and, even prior to the IRA's enactment, it was challenging to make the business case to invest in therapies for rare disease, which is even more complex than for more common conditions. Challenges include: enrolling sufficient patients given small patient numbers, uneven distribution of disease across populations, and heterogeneity of disease; designing clinical trials due to difficulties designating an appropriate comparator and challenges obtaining sufficient data from a small patient population; and

[7] SSA § 1194(e)(2)(D).
[8] EveryLife Foundation, The National Economic Burden of Rare Disease Study, February 2021, *available at:* https://everylifefoundation.org/wp-content/uploads/2021/02/The_National_Economic_Burden_of_Rare_Disease_Study_Summary_Report_February_2021.pdf.

obtaining high-quality patient data necessary to evaluate clinical trial outcomes given diversity in clinical presentation, disease progression, and other patient characteristics.

Given the extensive challenges rare disease patients face, and the difficulties of developing therapies in this area, CMS should consider a selected drug as addressing an unmet need even if there are existing therapies where: (1) the existing therapies have limited beneficial impact on quality or length of life and/or have significant side effects; and (2) the selected drug represents an improvement over those existing therapies. Similarly, certain therapies may work only for a subset of patients; a selected drug that fills these gaps and broadens the population of treatable patients should also be considered to address an unmet need.

However, CMS should not define unmet need from a narrow clinical perspective. For example, some therapies represent a significant advance in terms of convenience or reduced patient or caregiver burden (e.g., less frequent administration). From the perspective of rare disease patients and their caregivers, a therapy that overcomes any of these limitations of existing therapies unquestionably addresses an unmet need. To enhance the quality and utility of the information considered regarding unmet needs, CMS must therefore collect a broad array of both clinical and non-clinical information regarding unmet needs satisfied by selected drugs.

Finally, the determination of unmet medical need must also be indication specific. It is entirely possible that a single medication used in different indications may address an unmet medical need in one indication and not in another. CMS would enhance the quality and utility of the information to be collected by expressly soliciting information as to whether a selected drug meets an unmet need on an indication-specific basis, as it proposes to do for other aspects of this information solicitation.

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We thank CMS for considering our comments. Please contact Lisa Feng at lisa.feng@alexion.com if you have any additional questions about our comments.

Sincerely,

Lisa Feng, Senior Director, Health Policy
Alexion, AstraZeneca Rare Disease

Cc: Lara Strawbridge, Deputy Director for Policy, Medicare Drug Rebate and Negotiations Group, CMS

Greg Portner
Senior Vice President

Global Government Affairs & Policy
601 Thirteenth Street, NW
Suite 1100 North
Washington, DC 20005
Phone: 202.585.9649
Fax: 202.585.9730
Email: gportner@amgen.com
www.amgen.com

May 22, 2023

VIA ELECTRONIC DELIVERY

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building
Room 445-G
200 Independence Avenue, SW
Washington DC 20201

Re: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

Dear Administrator Brooks-LaSure:

Amgen Inc. (Amgen) appreciates the opportunity to submit comments on the Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) ("Data Elements ICR") posted on the Centers for Medicare & Medicaid Services (CMS) website on March 21, 2023.

Amgen is committed to using science and innovation to dramatically enhance people's lives, improving access to drugs and biologics (collectively, "drugs," consistent with CMS's convention), and promoting high-quality care for patients. Amgen develops innovator medicines and biosimilar biological products. Thus, our interest is to ensure a robust market for, and improve patient access in the United States to, both innovator and biosimilar biological products.

Amgen also supports the comments of the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO).

I. OVERARCHING CONCERNS

As an initial matter, Amgen remains extremely troubled that manufacturers will be compelled to participate in the Maximum Fair Price (MFP) program at all, including with respect to the Data Elements ICR that is the focus of this letter. The "negotiation" contemplated by the IRA is a negotiation in name only; it bears no resemblance to a traditional arms' length commercial

agreement. To the contrary, the IRA requires manufacturers to submit data in order to help CMS prepare for the "negotiation" and even dictates the format in which such data must be provided. This is all on pain of significant monetary penalties (CMPs) for failure to comply. Then, once CMS communicates an offer, manufacturers are restricted to making a counteroffer that is based only on certain factors listed in the statute. And all of this occurs against the threat of a crippling excise tax if the "negotiation" does not succeed. Any resulting "agreement" cannot be the result of a fair process and will in no way represent an agreed-upon mutual understanding between manufacturers and CMS.

Even assuming the IRA did not so coerce manufacturers, however, the data elements, including as addressed in the Data Elements ICR, present significant challenges and create inefficiencies. For instance, it will be impossible or infeasible for manufacturers to produce some of the information described the Data Elements ICR because manufactures would need to submit information that, though highly sensitive, is inappropriate and unnecessary for setting the MFP. Further, the data elements are requested in a manner that will generate unprecedented levels of burden for reporting to a government agency within an unrealistic timeline to appropriately address and verify in the format requested. This is particularly inappropriate given the excessive CMPs that can be imposed for failure to comply.[1] While we have tailored this letter to these and other concerns about the Data Elements ICR itself, in an attempt to engage in good faith with the opportunity to comment on the Data Elements ICR, we believe the entire process and law, of which the data elements are only a part, is fundamentally flawed.

CMS should publicly announce that the agency will take a flexible approach to data submission and enforcement, particularly in the early years of the program

In the Data Elements ICR, CMS has proposed incredibly detailed, burdensome, and, in many cases, confusing submission requirements for manufacturers. Furthermore, these requirements are supported by scant agency knowledge and experience, considering that this is the first year of the Maximum Fair Price (MFP) program and no comparable data collection has been carried out in the U.S. or, to our knowledge, anywhere in the world. Backing up these compelled disclosures are CMPs of $1 million per day.[2]

Moreover, many manufacturers may not be able to produce the information in the form and manner CMS has proposed. For example, in our comments below, Amgen has flagged several areas of concern, including research and development (R&D) costs specific to "[Food and Drug (FDA)]-approved indications" (Instructions to Section C), R&D costs for "failed or abandoned" products (Question 5), and product-specific federal financial support (Definitions for Section E).

In light of these issues, we recommend that CMS adopt a flexible approach to data collection, such as expressly allowing manufacturers to use reasonable assumptions and be open to communicating with manufacturers and working through submission challenges. We also urge the agency not to seek to impose CMPs where the manufacturer has submitted data to CMS in good faith. Publicly announcing these principles would help create a more cooperative environment.

[1] Social Security Act (SSA) §1197(b).
[2] *Id.*

The Data Elements ICR does not comply with the Paperwork Reduction Act (PRA)

Under regulations promulgated by the Office of Management and Budget (OMB), agency collection of information requests must demonstrate that the agency has taken:

> "every reasonable step to ensure that the proposed collection of information:
>
> > (i) Is the least burdensome necessary for the proper performance of the agency's functions to comply with legal requirements and achieve program objectives;
> >
> > (ii) Is not duplicative of information otherwise accessible to the agency; and
> >
> > (iii) Has practical utility. The agency shall also seek to minimize the cost to itself of collecting, processing, and using the information, but shall not do so by means of shifting disproportionate costs or burdens onto the public."[3]

The Data Elements ICR fails to satisfy each of these three requirements.

With respect to 5 C.F.R. § 1320.5(d)(1)(i) and (ii), we urge CMS to scale back the mandatory data submission requirements so that the agency: a) collects only information that the Department of Health and Human Services and other federal agencies do not already possess and b) permits manufacturers to submit information maintained in the usual course of business, rather than creating new data solely for the purpose of the MFP program, particularly in cases where it is not clear why data maintained in the usual course of business would not satisfy the needs of CMS.

In our comments that follow, we identify specific data elements that CMS should eliminate or modify to mitigate the burden on manufacturers without limiting CMS's ability to administer the MFP program.

In the "duplication of efforts" section of the Supporting Statement of the Data Elements ICR, CMS appears to try to sidestep the requirements of 5 C.F.R. § 1320.5(d)(1)(i) and (ii) regarding both burden and duplication by stating:

> "Some manufacturer-specific data described in sections 1193(a)(4) and 1194(e)(1) of the [Social Security Act (the Act)] may already be collected by CMS from manufacturers. However, the Act requires that manufacturer-submitted data must be obtained from the Primary Manufacturer."[4]

This is not actually the case. In no place does the IRA state that CMS cannot rely on data that it already possesses in lieu of obtaining it from manufacturers. Given the Paperwork Reduction Act and other initiatives by Congress and the federal government to reduce unnecessary regulatory burden, CMS should not read into the IRA a limitation that does not exist.

Moreover, the mandatory disclosure provisions of the IRA cited by CMS are best read as authorizing CMS to obtain information that it does not have. Under section 1194(e)(1),

[3] 5 C.F.R. § 1320.5(d)(1)(i)-(iii).
[4] Data Elements ICR, Supporting Statement at 4.

manufacturers that are compelled to participate in the MFP program must submit in the following general categories:

- Research and development costs of the manufacturer for the drug and the extent to which the manufacturer has recouped research and development costs.
- Current unit costs of production and distribution of the drug.
- Prior Federal financial support for novel therapeutic discovery and development with respect to the drug.
- Data on pending and approved patent applications, exclusivities recognized by the [FDA], and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act for the drug.
- Market data and revenue and sales volume data for the drug in the United States.

Other than the fourth category, these are all categories of information that the government does not possess. For example, manufacturers historically have reported limited information on cost inputs to the government. In contrast, manufacturers already report detailed pricing information to the federal government, such as information related to average sales price, average manufacturer price, and best price, which is presumably why section 1194(e)(1) does not expressly reference pricing data. In the Data Elements ICR, CMS characterizes this pricing information as "market data and revenue and sales volume data." Setting aside whether it is reasonable to interpret the phrase "market data and revenue and sales volume data" to include pricing data, it is not reasonable for CMS to take the position that the IRA requires that this information must be obtained from manufacturers as a mandatory submission under the MFP program, as to do so would be "duplicative of information otherwise available to the agency" and unnecessarily burdensome.

Furthermore, section 1194(e)(1)(D) merely requires "[d]ata on" patents, exclusivities, and FDA approvals, suggesting that Congress felt that manufacturers were in the best position to catalogue the relevant information for CMS.[5] However, there is no reason to believe that Congress intended for manufacturers to produce actual patent applications, FDA submissions, and approval letters, all of which are readily accessible to the government.

With respect to 5 C.F.R. § 1320.5(d)(1)(iii), the Data Elements ICR is incredibly broad and burdensome, with no apparent "practical utility" as to how CMS would use most of the information for price setting. For example, in the Data Elements ICR, CMS proposes to require manufacturers to provide an extensive list of confidential commercial information characterized as "market data and revenue and sales volume data,"[6] yet, in its March 15, 2023 guidance document (MFP Guidance), CMS struggles to explain how it will use this data, other than indicating that "if the average commercial net price is lower than the preliminary price, CMS may consider adjusting the preliminary price downward."[7]

[5] *Id.*§ 1194(e)(1)(D).
[6] Data Elements ICR § G.
[7] Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments, § 60.3.4 (March 15, 2023).

Another example is that CMS is proposing to require disclosure of a poorly defined category of information labeled "U.S. commercial average net unit price– best."[8] Manufacturers already expend significant resources to report "best price" under the Medicaid Drug Rebate Program and CMS provides no rationale as to why it needs manufacturers to calculate and report this additional best price.

CMS also provides no explanation as to why it would mandate disclosure of "quarterly total U.S. unit volume."[9] As the IRA is a Medicare-only price setting program, it is not obvious why CMS needs manufacturers to report non-Medicare unit volume. Even if one could guess at potential uses for such information, this is sensitive, potentially market-moving information that manufacturers should not be disclosing to CMS, or any third-party, without good reason.

Under 5 C.F.R. § 1320.5(d)(1)(iii), information collections must be limited to information that has "practical utility." CMS has not met this requirement with respect to the Data Elements ICR.

Finally, Congress did not give CMS carte blanche in the IRA. Under section 1193(a)(4)(B) of the SSA, CMS may require manufacturers to submit "information that the Secretary requires to carry out" the agency's price setting activities. In order for CMS to be authorized to mandate disclosure of information, CMS must articulate why the agency "requires" such information for the MFP program—or, in other words, why it has "practical utility." It has failed to do so in both the MFP Guidance and the Data Elements ICR, and thus, mandating the submission of this information is not only contrary to OMB regulations but also inconsistent with the IRA.

Other principles for all data elements

Data elements required to be submitted by manufacturers should reflect the following principles, in order to streamline and reduce the administrative burden placed on Primary Manufacturers:

- *Consistency with other agency reporting requirements*. Data elements such as non-federal average manufacturer price (non-FAMP) should be reported in a manner identical to how manufacturers are required to report to other government agencies in order to save time and labor costs on re-formatting for selected drug submissions given the short turnaround time requested.
- *Flexibility to supplement timely submissions*. CMS should provide manufacturers the option to supplement their submissions after the October 2, 2023 deadline if new data, documentation, or other substantive developments arise. Given the 30-day deadline established by the IRA and the massive amounts of data involved, manufacturers, as a practical matter, likely will be unable to provide all of the requested data. It would benefit both CMS and manufacturers for CMS to allow manufacturers to supplement their submissions, although we recognize that the IRA requires that manufacturers submit by October 2 some minimum amount of information in the five categories under section 1194(e)(1) of the SSA.
- *No word limits*. Throughout the ICR, CMS provides extremely limited space in the data fields via word and citation limits. Given the scope of these requests, and the lack of clarity in many of the terms applicable to the information to be collected, manufacturers may require additional space to adequately address these requests.

[8] Data Elements ICR § G.
[9] *Id.*

II. COMMENTS ON SPECIFIC DATA ELEMENTS

Section B. Non-FAMP Data Collection

Amgen recommends that CMS use the annual non-FAMP already reported by manufacturers to the U.S. Department of Veterans Affairs (VA) as defined in 38 U.S.C. § 8126(h)(5).[10] The annual non-FAMP is calculated using data from the 12-month period that aligns with the federal fiscal year (October 1-September 30). For 2021, this would be the annual non-FAMP value reported to the VA by November 15, 2021, calculated using transactions from October 1, 2020 through September 20, 2021. As discussed above, this would be consistent with 5 C.F.R. § 1320.5(d)(1)(i) and(ii), which requires CMS to make every reasonable effort to ensure that information collected is "the least burdensome necessary for the performance of the agency's functions" and "[i]s not duplicative of information otherwise accessible to the agency."[11] We also ask that manufacturers have the ability to make timely restatements.

Amgen further requests that CMS clarify that the units for non-FAMP may be different from the units on the Part D Prescription Drug Event record, which uses National Council for Prescription Drug Program defined values. CMS should recommend that manufacturers report the unit measure for non-FAMP in the explanatory field for Section B. More specifically, for all pricing metrics, the unit the manufacturer reports should match the unit used in the original metric. Due to the burden on respondents, as well as the CMP implications and related exposure, CMS must perform any cross-walking necessary.

Section C. Research & Development Costs and Recoupment

General Comments

CMS should provide manufacturers the option to attest that R&D costs have been recouped

Providing data in response to CMS's proposed detailed definition of R&D costs, broken into six specific categories, would impose an immense burden on manufacturers. We are concerned that CMS is under the impression that manufacturers track and maintain R&D cost information at a level of detail that does not correspond with the ordinary course of business of manufacturers. An attempt at compliance would require Amgen to review prior expense records and retrospectively flag them by product and CMS R&D cost category. It may prove to be an impossible task to assemble and submit accurate information, but, even if did not, it would be immensely time consuming, expensive, and burdensome. It would be even more challenging for older products, such as those subject to the MFP program, and products acquired through merger or acquisition. That the challenges of assembling this data will vary according to products—not to mention across manufacturers—makes it extremely unlikely that CMS will ever receive data homogenous enough to allow for meaningful analysis (assuming that is what CMS intends to do).

Such burdensome requirements are not necessary for CMS to carry out the MFP program. In the MFP Guidance, CMS appears to be proposing to consider only the binary question of whether the manufacturer has recouped total R&D costs related to the product, stating that it will

[10] 38 U.S.C. §8126(h)(5).
[11] 5 C.F.R. §1320.5(d)(1)(i), (ii).

consider adjusting the initial offer price upward or downward based on whether the manufacturer has recouped its costs.[12]

To accomplish the same policy purpose while mitigating burden on manufacturers, CMS should give manufacturers the option to attest that they have recouped R&D costs.

CMS should not finalize its proposal to require reporting of R&D costs in six categories

If manufacturers are to report drug-specific costs, we ask that CMS permit total R&D costs, not broken down by category. Again, there is apparently no policy purpose behind the six categories, it would be burdensome to divide costs in this artificial way, and we believe that overall, it will result in confusion and less accurate reporting.[13]

For products acquired by a manufacturer, CMS should permit manufacturers to report as R&D costs acquisition costs attributable to R&D

In the Data Elements ICR, CMS instructs manufacturers to exclude acquisition costs.[14] This is an ill-conceived policy that CMS should reverse when it issues its final guidance document. Given that, in the MFP Guidance, CMS proposes to adjust the initial offer price upward or downward based on whether the manufacturer has recouped R&D costs, it appears that CMS believes that molecules developed in-house should be assigned greater value than products that have been acquired. This distinction makes no business sense. Manufacturers such as Amgen are constantly investing in their internal R&D as well as evaluating opportunities to "buy R&D" through external acquisitions. In either case, the value of the therapy is the same to patients, health care providers, and payers. The product may also be of greater benefit to patients in the hands of an acquiring company if the company has better capability to market and manufacture a reliable supply of the product. Furthermore, when developing reasonable allocation methodologies related to R&D costs, a manufacturer would never exclude acquisition costs because such an approach would understate, in some cases drastically, the manufacturer's investment.

Instructions for Section C

Manufacturers should be permitted to include costs for label-enabling research

If CMS moves forward with mandating disclosure of product-specific information and with requiring detailed categorization of R&D costs, we ask that CMS explicitly broaden the definition of R&D costs to include costs incurred for label-enabling research and for ongoing research.

The Data Elements ICR proposes that R&D costs include only costs "incurred by the Primary Manufacturer for all FDA-approved indications of a drug...."[15] Read narrowly, limiting R&D costs to those incurred for "FDA-approved indications" would fail to reflect the breadth of significant R&D investment that many manufacturers make in approved drug products. Manufacturers may

[12] MFP Guidance § 60.3.4.

[13] Amgen also would support the two alternative options proposed by PhRMA: 1) allowing manufacturers to allocate a percentage of total R&D to the selected drug based on a generally accepted standard and 2) allowing manufacturers to provide data in two broader categories: a) costs of R&D *before* initial FDA approval and b) costs of R&D *after* FDA approval, which would include Phase IV costs, allowing for reasonable assumptions and allocations of spending for the selected drug.

[14] Data Elements ICR §C.

[15] *Id.*

routinely incur R&D costs concerning new routes of administration, dosing regimens, delivery devices, or other uses that improve patient experience or convenience. While this research may not result in a new FDA-approved indication, such new conditions of use are reflected in the drug labeling. We therefore urge CMS to explicitly permit manufacturers to submit R&D costs associated with all label-enabling New Drug Application (NDA) or Biologics License Application (BLA) supplements. We recommend that CMS permit manufacturers to submit such cost information in response to Question 6 ("All Other R&D Costs").

Perhaps more importantly given the CMPs associated with manufacturer-reported data elements, Amgen does not track R&D costs based on whether it specifically resulted in an "FDA-approved indication," and it would be infeasible or impossible to reconstruct this information, so we would likely be unable to provide the information in the form requested.

CMS should permit manufacturers to include costs for ongoing research

The Data Elements ICR also states that CMS intends to exclude from R&D costs the "costs associated with ongoing basic pre-clinical research, clinical trials, and pending approvals."[16] Ongoing research and clinical trials frequently result in new uses that meaningfully contribute to the value offered by a drug. Such research may later result in an approval—a category of cost included in the proposed R&D cost definition—yet CMS proposes to preclude a manufacturer from including ongoing costs simply if a drug happens to be selected for negotiation before completion of the research. We request that CMS permit manufacturers to include ongoing research when reporting R&D costs.

Question 5

CMS should not differentiate between successful and "failed or abandoned" products

As Amgen currently tracks R&D costs, all discovery and preclinical developmental costs are categorized the same (and, under framework of the Data Elements ICR, would be reported under Question1) and we do not differentiate between molecules that were later studied in clinical trials and "products with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials."[17] In fact, it is inappropriate at the pre-clinical stage to make distinctions between "products" because the end-result "product" may not be clear at this early stage because critical details including routes of administration and dosing regimens may be determined through clinical trials.

Question 6

CMS should clarify that it is appropriate for manufacturers to include royalty payments attributable to R&D costs in this category

In cases where rights to a product are split between multiple manufacturers, agreements between manufacturers may require royalty payments attributable to R&D costs. We believe such costs should be reported in response to Question 6, and we ask that CMS expressly clarify this.

[16] *Id.* § C, Instructions.
[17] *Id.* § C, Question 5.

Question 7

CMS should choose whether to consider R&D costs and revenue on a global or U.S. basis and be consistent

CMS has proposed to *include* in the total lifetime net revenue calculation the "global, total lifetime net revenue"[18] yet *exclude* from R&D costs any "costs associated with receiving foreign approvals."[19] This lack of symmetry in the assessment of revenues versus expenses inappropriately disadvantages manufacturers. It essentially penalizes manufacturers for international sales while failing to recognize a manufacturer's investment in research that supported the approvals that enabled such marketing. As a matter of consistency and as but one step toward fairness, CMS should adopt a uniform approach to inclusion (or exclusion) of international revenues and expenses.

Section D: Current Unit Costs of Production and Distribution

Instructions for Section D

Sales and marketing costs should be included as costs of distribution

Under the Data Elements ICR, CMS proposes to exclude "marketing costs" from the definition of "current unit costs of production and distribution of the selected drug."[20] We believe this apparent bias against sales and marketing is misplaced. After FDA approves a product, patients may not see the benefit of it unless manufacturers expend resources to educate health care providers (through disease state education, and information regarding the safety and efficacy of the product itself, and patient support services) and to negotiate with payers for access to the product. These functions are critical to create awareness of the disease and the product's efficacy so that the product reaches appropriate patients. Excluding marketing costs creates an inaccurate picture of the full costs of production and distribution related to a product.

Manufacturers should report liquid injectable units based on weight rather than volume

Amgen assesses production costs per unit for liquid injectable drugs using micrograms or milligrams, which reflects the ingredient weight. We believe this is also the industry standard.

In the Data Elements ICR, CMS is proposing that manufacturers report costs using liquid volume, referencing the National Council for Prescription Drug Programs (NCPDP) Billing Unit Standards.[21] As suggested by the title, the NCPCP standards were developed for billing purposes and, in fact, providers typically bill payers for injectables using milliliter-based units. But they do not reflect current industry practices for tracking costs per unit. Accordingly, CMS should switch to weight-based reporting when it finalizes its reporting guidance.

[18] *Id.* § C, Question 7.
[19] *Id.* § C, Instructions.
[20] *Id.* § D, Instructions,
[21] *Id.*

CMS should permit manufacturers to determine the most appropriate 12-month period for reporting costs

CMS proposes that manufacturers report average unit costs during the 12-month period ending May 31, 2023.[22] Manufacturers are unlikely to track information in this way, instead typically using a calendar or fiscal year approach. There seems to be little or no benefit to CMS prescribing such an unusual reporting period, given the burden it would impose on manufacturers. Therefore, CMS should allow manufacturers to determine their own period based on current business practices.

Manufacturers should have flexibility to align allocation between production and distribution with existing business practices

Certain aspects of CMS's definitions of "costs of production" and "costs of distribution" are inconsistent with Amgen's existing business practices. For example, Amgen treats packaging, packaging materials and labeling as costs of production, but these costs are defined as costs of distribution under the Data Elements ICR.[23] Given that whether a cost is categorized as a production or distribution cost has no bearing on CMS's price setting activities, and to mitigate unnecessary burden, CMS should permit manufacturers to characterize production and distribution costs consistent with usual business practices.

Section E: Prior Federal Financial Support

General Comments

Disclosure should be limited to Government Interest Statements

We encourage CMS to limit the data disclosure requirements for prior federal financial support to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency.

CMS should establish a defined look back period

We encourage CMS to narrow the relevant time period for this request to federal financial support received within the last 10 years of the BLA/NDA approval. As currently written, the time period starts at the beginning of the research and development program,[24] which for some drugs, will have occurred more than 30 years ago, and in some instances by a predecessor company that no longer exists. This would seemingly require companies to try to track down financial and tax records for several decades and perhaps well before this type of data was routinely kept in electronic form. It is unclear whether companies could meet this request without limiting the time frame.

[22] *Id.*
[23] *Id.*
[24] *Id.* § E, Definitions.

Definitions for Section E

CMS should not require manufacturers to provide the "federal financial support" data on a product-specific basis

Under the Data Elements ICR, CMS proposes to define "federal financial support for novel therapeutic discovery and development" to include tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and development "related to the selected drug."[25] We urge CMS to reconsider this request, and instead require disclosure only of Government Interest Statements, because companies do not typically track financial or tax credits on a product-by-product basis. In fact, there is not any meaningful way to calculate such product-specific taxes or credits given that the amount of taxes or credits potentially associated with one product is highly interdependent on what happens with other products and aspects of the business.

Section F: Patents, Exclusivities, and Approvals

Definitions for Section F

CMS should limit disclosure to patents directed to the active ingredient

We encourage CMS to limit the data disclosure requirements to only those patents and patent applications with a specific claim directed to the active ingredient of the selected drug, rather than more generic patents that, for example, cover a specific manufacturing process, a process for purifying a drug substance, or a process of formulating a drug substance that could be used to manufacture a number of different pharmaceutical products.

CMS should clarify the definitions and instructions for Section F to promote clarity and accuracy

We have the following recommendations for the definitions under Section F:

- The definitions section states that exclusivity refers to certain delays and prohibitions on the approval of competitor drugs "that attach upon approval of a drug."[26] CMS instead should refer to exclusivity attaching upon "approval of an NDA/BLA or approval or submission of a supplement to such application." Some types of regulatory exclusivity, including orphan exclusivity and new clinical investigation exclusivity, may attach upon FDA approval of a supplement after initial approval of a drug. In addition, pediatric exclusivity may attach after submission of a supplement reporting results of pediatric testing.
- According to the definitions section, the phrase "active and pending FDA applications and approvals"[27] would include "all applications for approval" under specified federal statutes. We recommend that CMS clarify that the phrase "applications and approvals" includes "all applications or supplements." Inclusion of supplements is appropriate and appears to be consistent CMS's intention. Omission of the word "supplements" may cause unnecessary confusion.

[25] *Id.* § E, Definitions, Question 10.
[26] *Id.* § E, Definitions.
[27] *Id.*

- With respect to the definition of applications and approvals, we also suggest that CMS state that manufacturers need only list potential label-enabling supplements and approvals. We request that CMS explicitly exclude manufacturing or other chemistry, manufacturing, and controls supplements. A manufacturer may submit numerous manufacturing-related supplements over the life of a drug. Providing a detailed listing would be burdensome to manufacturers while offering little-to-no value to CMS during the price negotiation process.

Instructions for Section F

The period for reporting FDA exclusivities and approvals should explicitly include dates of supplements

The instructions provide that for Questions 13 through 16, the time period for reporting "ends on the date the most recent NDA/BLA was approved for the selected drug."[28] We recommend amending the instruction so that the reporting period ends on the date that "the most recent NDA/BLA *or supplement* was approved for the selected drug." Adding the reference to a "supplement" would more clearly capture situations where orphan exclusivity, pediatric exclusivity, and new clinical investigation exclusivity are earned based on submission of a post-marketing supplement.

Question 13

Manufacturers should not be required to upload patent applications

In the table under Question 13, CMS appears to be proposing to require that manufacturers upload patent applications. We question what purpose a patent application might serve in CMS's price setting process. That said, to the extent there is relevant information contained in a patent application, CMS should obtain it directly from the Patent and Trademark Office (PTO). Requiring manufacturers to upload patent applications would be unnecessarily burdensome for manufacturers because older applications may not be available in electronic format, especially considering the 30-day turnaround time to submit data. The government already has access to patent applications through the PTO. CMS therefore should obtain patent applications from PTO to the extent they are necessary to the MFP program.

Question 15

CMS should acknowledge uncertainties regarding expiration of regulatory exclusivity

Question 15 asks that manufacturers list each type of applicable regulatory exclusivity and the corresponding "Exclusivity Expiration Date."[29] Not every licensure of a biological product is considered a "first licensure" that qualifies for its own 12-year exclusivity period. Whereas FDA's Orange Book and Purple Book provide authoritative information on the date of expiration of many types of regulatory exclusivity, FDA does not routinely proactively publish in the Purple Book (or otherwise) determinations about Reference Product Exclusivity for Biological Products or the date of expiration. We recommend that CMS acknowledge that in some cases there may be some

[28] *Id.* § E, Instructions.
[29] *Id.* § E, Question 15.

uncertainty as to whether a particular product has received 12-year Reference Product Exclusivity and ask manufacturers to provide their best judgment as to the expiration date of such exclusivity.

Question 16

The "submission number" column should be deleted

Question 16 prompts manufacturers to include a "submission number"—in addition to an "application number"—for all active and pending applications and approvals.[30] It appears that "submission number" intends to refer to the numbers used internally by manufacturers to track their submissions in serial order. We believe that this number would have no meaning to CMS. We ask that CMS remove this field from Question 16.

Section G: Market Data, Revenue, and Sales Volume Data

Questions 21 (340B Ceiling Price), 27 (Federal Supply Schedule), and 29 (Big Four)

We ask CMS to clarify which units should be included

For each of these three questions, it is not clear whether manufacturers should report: 1) all units subject to the ceiling price under the program, whether they are sold for the ceiling price or a lower, sub-ceiling price or 2) only units actually sold at the ceiling price. CMS should clarify the information it is seeking so that all manufacturers will provide consistent information.

Question 33

CMS should strike the column "Manufacturer Average Net Unit Price to Part D Plan Sponsors-Without Patient Assistance Programs"

The HHS Office of the Inspector General (OIG) has made clear that manufacturers may not offer copay assistance to Part D enrollees,[31] and manufacturers do not currently provide such assistance to Medicare beneficiaries. Accordingly, there is no need for this column under Question 33.

Questions 37 and 38

CMS should delete these questions because they are redundant to Question 19

In Question 37, CMS requests data on unit type and volume by quarter for five years by National Drug Code. In Question 19, CMS asks for the same information, plus Wholesale Acquisition Cost. CMS should delete Questions 37 and 38, so manufacturers are not required to provide the same information twice.

[30] *Id.* § E, Question 16.

[31] See, e.g., OIG Special Advisory Bulletin: Pharmaceutical Manufacturer Copayment Coupons (September 2014).

Section H: Evidence About Alternative Treatments

Instructions for Questions 40 through 43

CMS should clarify that it will consider quality of life data

Consistent with the prohibition against certain uses of Quality of Life Years (QALYs) under section 1194(e)(2) of the Act, CMS instructs submitters not to "include as evidence comparative clinical effectiveness research that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill." [32] However, it is important that CMS clarify that submitters may submit, and CMS will consider, evidence regarding the impact of a therapy on quality of life, provided that it does not treat extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

Question 40

CMS should seek input on the selection of therapeutic alternatives

In this question, CMS requests information regarding prescribing information with respect to therapeutic alternatives of a selected drug,[33] but it is unclear how CMS will identify therapeutic alternatives and to what extent manufacturers and other stakeholders will be permitted to comment on them. To minimize burden of submission and increase likelihood that the information submitted to CMS is relevant and useful, CMS should publicly identify the therapeutic alternative, as well as any resources (e.g., clinical guidelines) it relied upon to identify the therapeutic alternative, on which it seeks information in response to Question 40 and communicate this information at the same time it announces the products selected for the MFP program. We also request that CMS seek input with respect to whether it has selected the appropriate therapeutic alternatives, either through Question 40 or otherwise.

The word limit is insufficient

As discussed above, there should be no word or character limits for any of the explanatory fields in this information collection, particularly in early years of the MFP program as CMS learns the types and quantity of information that is helpful to administration of the program. If CMS decides to finalize a word limit, we request that CMS increase the 1,000 word limit to 5,000 for Question 40 given the breadth of information available for selected drugs that have been studied for several years and have several indications.

Question 41

CMS should clarify that submitters are not required to submit information regarding all indications

As currently proposed, respondents are asked to submit all information on all potential comparators across all indications within the 30-day deadline, with no bounds on the potential universe of products.[34] We request that instructions be updated to confirm that data for every

[32] Data Elements ICR § H, Instructions.
[33] *Id.* § H, Question 40.
[34] *Id.* § H, Question 41.

indication for the selected drug is not required. This will allow manufacturers to focus the available word count on the priority indications where the selected drug is most commonly used.

The word and citation limits are insufficient

If CMS decides to finalize a word limit, we request that CMS increase the 3,000 word limit to 10,000 for Question 41 given the breadth of information available for selected drugs that have been studied for several years and have several indications. Likewise, CMS should increase the citation limit from 50 to 200.

Question 42

The word and citation limits are insufficient

If CMS decides to finalize a word limit, we request that CMS increase the 3,000 word limit to 10,000 and increase the citation limit from 50 to 200.

Question 43

The word and citation limits are insufficient

If CMS decides to finalize a word limit, we request that CMS increase the 1,000 word limit to 5,000 and increase the citation limit from 50 to 200.

* * * * *

We appreciate your consideration of our comments on the Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) ("Data Elements ICR"). Please contact Giana Mandel by telephone at (571)-228-6637 or by e-mail at gmandel@amgen.com if you have any questions about our comments.

Regards,

Greg Portner

Senior Vice President

Global Government Affairs and Policy

BY ELECTRONIC SUBMISSION VIA REGULATIONS.GOV

May 22, 2023

Meena Seshamani, M.D., Ph.D
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health & Human Services
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

Dear Deputy Administrator Seshamani,

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialization of prescription medicines, primarily for the treatment of diseases in three therapy areas – Oncology, Cardiovascular, Renal & Metabolism (CVRM) and Respiratory & Immunology. We are also working to solve the challenges for rare disease patients through our subsidiary Alexion. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

While AstraZeneca remains troubled about the impact the *Inflation Reduction Act* could have on the development of future medicines and patient access to the latest cures, we will comply with the law and appreciate the opportunity to submit comments in response to the above captioned Information Collection Request (ICR) setting forth the proposed information submission requirements for selected drugs in the Medicare Drug Price Negotiation Program (Negotiation Program) to the Centers for Medicare & Medicaid Services (CMS) for initial price applicability year (IPAY) 2026. AstraZeneca is an innovative company that supports value-based care and evidenced-based decisions.

Executive Summary and Our Global Perspective

We urge CMS to deploy a multifaceted consideration of a selected drug's clinical value as the basis of any evaluation using the following core value principles:

1. **Transparency:** Using scientific principles, consistent methodology, and appropriate evidence, various stakeholders should be able to come to similar conclusions.

2. **Consistent methodology with consideration of contextual factors:** Having a consistent methodology that considers clinical and other factors is particularly important for oncology, rare diseases, and other diseases with high unmet need. Assessments of rare

disease and oncology treatments require special consideration of the study recruitment challenges, lack of disease-specific endpoints, and other factors that shape the evidence which would ultimately inform value assessment.

3. **Selection of appropriate therapeutic alternatives:** Therapeutic alternatives should be based on clinical, not economic factors, and should be limited to FDA-approved treatments within the targeted patient population and line of therapy.

4. **Holistic perspective:** The definition of value should include patient-experience factors, impacts on population health equity, healthcare system resource utilization, and societal impacts outside the healthcare system.

5. **Consideration of a broad spectrum of data sources:** In addition to clinical trial data, value assessments should include data from patient registries and other real-world data sources.

In general, AstraZeneca is concerned the ICR reporting requirements are misaligned with the Paperwork Reduction Act (PRA) and impose overly burdensome requirements on manufacturers. The complexities of the Negotiation Program submission requirements as currently outlined by CMS cannot be collected and reconciled within the required timelines. We urge CMS to simplify the data requirements by allowing for reporting through attestations, such as for R&D cost recoupment, as well as allowing manufacturers to submit information in a manner consistent with how such data are typically tracked and recorded in other federal programs or under current accounting principles.

CMS is also proposing to limit its ability to fully understand selected drugs by confining submissions to a limited number of words, citations, and constrained data fields. Manufacturers should be allowed more flexibility to explain data elements using reasonable assumptions. Further, CMS should remove the word limits for responses to allow for a more complete narrative response and explanation of methods for data submissions. This will be especially important for questions related to therapeutic alternatives as the ICR provides a very limited number of questions and data fields while seeking information that encompasses multiple treatment options, multiple indications, and large volumes of evidence on a wide range of clinical and patient-centered outcomes that have accumulated through years of post-approval research.

As a global company, we have experienced how countries differ in the terms of how robust and transparent their decision-making processes are; they also utilize varying base methodologies—clinical efficacy and safety are key considerations for all countries. It is also critical to observe how strongly Health Therapeutic Assessment (HTA) entities adopt considerations for rare diseases and create alternate pathways for different types of assessments—some countries acknowledges specific considerations for orphan drugs, while countries dominated by cost-effectiveness struggle to provide access to particular types of innovation. For example, in one country there is a dedicated innovation assessment with a focus on unmet need and added therapeutic benefit. Conversely, the patient perspective is not a major assessment criterion used

by any foreign HTA entity and we recommend CMS address this gap in the development of the Negotiation Program.

Detailed Section-by-Section Comments

Section C: Research and Development Costs and Recoupment

The ICR requests a far broader and more detailed array of data than necessary, the proposed approach does not support a value-based assessment of product value. The specificity and novelty of CMS' six-part subdivision of R&D costs significantly increases the difficulty and burden of complying with this requirement.

AstraZeneca is concerned the level of granularity required for reporting R&D costs and recoupment is inconsistent with how life sciences companies and investors perceive and approach risk and risk-adjusted returns. CMS' reporting methodology is not consistent with how manufacturers track cost information, raising concerns for how companies can successfully comply with these requirements given the time and complexity required to calculate such costs. Furthermore, the data submissions requirements are overly burdensome and unnecessary for CMS to determine R&D recoupment under Section 1194(e)(1).

AstraZeneca is also concerned the statement that "all dollar figures submitted to CMS must be cash-outlay costs to the Primary Manufacturer" and "must exclude any costs to entities that are not the Primary Manufacturer." This language is too rigid for co-commercialized products and penalizes industry collaboration to bring new therapies to patients. While CMS recognizes the acquisition of another manufacturer is an investment and development cost, it explicitly excludes acquisition costs from the definition of research and development. AstraZeneca urges CMS to reconsider this narrow definition.

Similarly, research failures and associated costs outnumber successes, especially when compared to the number of products reaching the market. CMS allows sponsors to report costs associated with failed or abandoned drugs, but only those with the same active moiety/active ingredient or mechanism of action as the selected drug and direct *post-IND costs* for drugs in the same therapeutic class. Continued efforts to innovate in complex and difficult treatment areas is only possible if manufacturers spread the risk of research and development across their portfolio, both for successes and failures. CMS should consider the full costs of development and failures when assessing discovery and preclinical developmental costs and not overlook how many drugs switch therapeutic classes during the development process.

The definition of how manufacturers should treat FDA-mandated Phase IV trials is also limited. It is unclear why the Agency separately requires this information apart from other post-marketing trials. All post-marketing studies serve the purpose of providing more information about the value and safety of a therapy. CMS should consider the costs of all non-FDA mandated post-marketing studies.

To address the various concerns with reporting on R&D spending and recoupment, we recommend CMS amend the ICR to allow a single, global response for R&D costs similar to what manufacturers provide in Form 10K for Securities and Exchange Commission (SEC) filing.

CMS should also allow for a simple attestation (YES/NO) on cost recoupment. If a respondent stipulates "YES" that they have recouped research costs, CMS should not need any additional information. If a manufacturer checks "NO," the manufacturer should then provide an explanation.

Section D: Current Unit Costs of Production and Distribution

AstraZeneca is concerned with the broad, overly burdensome request which extends beyond the terms of the IRA. CMS should revise the ICR to provide discretion to manufacturers to describe production and distribution costs. The Agency should also clarify how unit costs will be incorporated holistically into a clinical value-based negotiation.

Specifically, Section D requires current unit costs of production and distribution in the US, while Section C requests recoupment of R&D using global, lifetime net revenue. These metrics cannot be compared on an "apples-to-apples" basis given one element measures revenue at a global scale across markets while the other measures cost within one market (i.e., the US). CMS has not made clear how it plans to standardize data comparisons, including in comparing global and US data points. The mixing of global and US data inputs will create distorted views of revenue-to-cost comparisons. We therefore urge CMS to compare US costs of production and distribution with US (rather than global) revenue figures.

In addition, Question 7 of the ICR includes language recognizing global total lifetime net revenue, exclusive of any royalty payments. However, Section D of the ICR does not include language that acknowledges royalties, revenue/profit shares, or other forms of revenue. If manufacturers only report revenue and CMS disregards other financial costs, then CMS has overstated how much manufacturers have recouped research and development costs. This is especially true of royalties based on revenue or other variables where R&D or other expenses are not shared.

AstraZeneca is concerned about the collection of per-unit cost of goods and services (COGS). Manufacturers generally do not report COGS in their financial statements, as COGS are highly variable over time. The Agency will receive better information if a range of COGS is permitted. This will allow manufacturers to provide more accurate data in a timelier manner, as manufacturers assess ranges of dynamic costs that will vary over time. In addition, it will allow the Agency and manufacturers to focus on the overall value of medicines, rather than arbitrary per-unit costs.

Finally, CMS should revise the Negotiation Program to provide discretion for manufacturers to describe production and distribution costs. As an international company, AstraZeneca operates an integrated and complex global supply chain. We do not currently track or record production costs at the NDC-9 level. Rather we focus on the overall value of the supply chain. It would be more appropriate for CMS to accept a narrative explanation from companies describing production and distribution costs given the variability across companies and products. If CMS moves forward with a specified methodology for production cost submissions, it will be difficult for companies to comply with the mandate without costly changes to existing accounting systems.

Section E: Prior Federal Financial Support
CMS strays far beyond the statute for this data element to collect data which is not relevant to a value-based negotiation process.

AstraZeneca is concerned CMS has chosen an overly broad definition of federal funding or collaboration in requiring submission of federal financial support. We strongly recommend limiting consideration of prior federal financial support to funding resulting in a patent application containing a Government Interest Statement and/or research where a patent assignee was a US government Agency for an invention directly related to the development of the selected drug (e.g., excluding basic science, research tools, or similar general concepts).

To comply with the PRA, CMS should obtain this information through other, already available sources, rather than procuring it entirely from manufacturers. In addition, the federal financial support chart should request only the total federal financial support figure, along with an explanation. The burden and difficulty of obtaining data in the specific manner CMS requests in the provided data fields significantly outweighs the utility of this data for the Negotiation Program.

Section G: Market Data, Revenue, and Sales Volume Data
There is no legitimate reason for CMS to request the pricing data as outlined in this ICR and we fail to see how this data collection will meaningfully support a value-based negotiation.

The only pricing metric the IRA indicates manufacturers must report to CMS under the Negotiation Program is non-FAMP. CMS should not use the general term "market data, revenue, and sales volume" to seek propriety pricing information across all market segments for a selected drug. These data points are not necessary or essential to the operation of the Negotiation Program.

CMS has requested manufacturers provide the 340B Ceiling Price and 340B Prime Vendor Program Price Medicaid Best Price, Federal Supply Schedule (FSS) Price, and the Big Four Price. AstraZeneca has two primary concerns with these requests. First, the Agency has access to these prices through existing government reporting requirements. Second, none of these pricing metrics have any bearing on price negotiation. CMS should only assess pricing metrics with direct bearing on Medicare price negotiation and avoid requesting data from peripheral government price metrics to which it already has access.

It is also unclear why CMS seeks 20 quarters of revenue and sales volume data. Reporting data from the previous five years would be extremely burdensome for manufacturers, especially regarding the average commercial price and average Medicare Part D price. As CMS is aware, average commercial price and average Medicare Part D price are not publicly reported metrics. This information would necessitate manufacturers to calculate new and unnecessary metrics, retroactively, while attempting to accurately comply with unit conversions. Any reporting of data should align to the units of measurement already required by other federal entities. CMS should bear the responsibility of converting unit types to ensure consistency.

Finally, AstraZeneca is deeply concerned about the reporting approach for Secondary Manufacturers. Primary Manufacturers legally do not have access to Secondary Manufacturer information. We are concerned this ICR contains unreasonable assumptions related to a Primary Manufacturer's ability to access data requested from Secondary Manufacturers. CMS should instead enter into separate legal agreements with each entity that satisfies the definition of a manufacturer to obtain any essential information.

Section H: Evidence About Alternative Treatments

As currently requested in the ICR, CMS does not provide adequate clarity or time for respondents to provide the information necessary for CMS to properly conduct and synthesize patient-centered clinical effectiveness research and costs of selected drugs and treatment alternatives for the purposes of a value-based negotiation.

AstraZeneca is broadly concerned by the significant uncertainty as to what types of clinical information CMS will prioritize as part of the evidence review. For example, it is unclear if CMS will focus on Randomized Control Trials (RCT), systematic reviews, or on Real World Evidence (RWE). It is also unclear how CMS will approach patient-reported outcomes (PROs). Many oncology and rare disease treatments lack head-to-head studies or rely on surrogate endpoints, and it remains unclear how CMS will approach these datapoints. AstraZeneca supports CMS' policy of not considering quality-adjusted life years (QALYs); however, we also recommend CMS require the removal of all QALY-based information from submissions. We further urge CMS to clarify how evidence standards will take account of contextual factors, including the disease itself and the rarity of the condition.

AstraZeneca is also highly concerned with CMS' approach to selecting therapeutic alternatives. To ensure a transparent and efficient process, it is important for manufacturers to have insight and understanding into how CMS will select therapeutic alternatives and notice of those alternatives once chosen by the Agency. Misalignment on the appropriateness of therapeutic alternatives during negotiation will introduce significant risks to the process and could create delays in data submissions— leading to additional work for CMS and increasing uncertainty in the negotiation process. At a minimum, AstraZeneca urges CMS to provide manufacturers with an opportunity to engage with Agency and review CMS' methodology for the selection of therapeutic alternatives before CMS makes such a determination.

CMS notes any organization or member of the public may submit data on therapeutic alternatives to drugs selected for negotiation. The Agency will accept these submissions via a public use section of the Health Plan Management System (HPMS). To ensure more appropriate evidence submissions, CMS should publicly identify the therapeutic alternative(s), as well as any evidence-based resources (e.g., clinical guidelines) it relied upon to identify the therapeutic alternative, on which it seeks information in response to Question 40.

Based on AstraZeneca's experience in global markets and our principles of transparent, predictable, evidence-based assessment and a focus on clinical value, we believe that patients benefit most when:

- Comparators reflect the most common alternative for Medicare populations

- Appropriate comparators have a licensed indication that covers the population of interest and accounts for disease context, particularly for rare diseases with limited available licensed options
- Robust data on clinical effectiveness is available to make comparisons
- Comparators are be based on clinical effect factors and not economic considerations

Additionally, we urge CMS to clarify its approach to comparators, whether at the disease level, indication level or population level.

Biomarker testing and other personalized medicine advances should also be considered when determining therapeutic equivalents, as targeted therapies frequently have a specific biomarker of focus for the therapy that may not be shared by others.

We also urge CMS to consider only on-label indications in selecting therapeutic alternatives, as off-label indications have significantly less robust data regarding safety and efficacy relative to on-label uses.

Summary and Conclusion

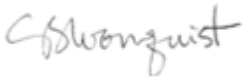
To strengthen its stated goal of increasing health equity, AstraZeneca urges CMS to weigh clinical factors more heavily than market data. Specifically, CMS should focus on whether a selected drug demonstrates a clinical benefit and addresses an unmet need. This approach would best preserve incentives for innovation, establish a clear and predictable methodology for determining drug pricing, and enable CMS to meet statutory obligations under the IRA. An over-emphasis on market data does not take into consideration the potential overall value, outcomes, and clinical benefits that are delivered to patients.

CMS should also expand the allowed amount of text and permit manufacturers to include graphical elements and tables to convey a more complete narrative regarding evidence about alternative treatments. Applying a word limit at a medicine level limits the ability of manufacturers of medicines with multiple indications to provide full and comprehensive information across all aspects of a therapy, its studies, and related clinical data.

* * * * * *

AstraZeneca thanks you for the opportunity to submit comments and looks forward to continuing to engage with CMS as it implements the Negotiation Program for IPAY2026 and beyond. I can be reached at 202-350-5542 or christine.bloomquist@astrazeneca.com with any questions.

Sincerely,



Christie Bloomquist
Vice President, US Corporate & Government Affairs

Biotechnology Innovation Organization
1201 New York Avenue NW
Suite 1300
Washington, DC, 20005
202-962-9200

May 22, 2023

Via Electronic Delivery
The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-10847
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Information Collection Request (ICR) for Negotiation Data Elements (CMS-10847)

Dear Administrator Brooks-LaSure:

The Biotechnology Innovation Organization (BIO) appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS's) Information Collection Request for Negotiation Data Elements under the Inflation Reduction Act (IRA).

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics yield not only improved health outcomes, but also reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

For purposes of negotiation of the maximum fair price (MFP), the statute (SSA 1194 (e)) directs CMS to consider the following factors:

- Manufacturer-specific data (SSA 1194 (e)(1)): Research and development costs and the extent to which the manufacturer has recouped such costs; current unit costs of production and distribution; prior federal financial support for discovery and development; and data on pending and approved

patents and exclusivity; and market data and revenue and sales volume data.

- Evidence about alternative treatments (SSA 1194 (e)(2)): the extent to which the drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such alternative; FDA-approved prescribing information for the drug and the alternatives; comparative effectiveness of the drug and the alternatives, including effects on specific patient populations; the extent to which the drug and the alternatives address unmet medical need.

Most fundamentally, and as we have noted in previous comments to the Agency, we believe CMS should emphasize factors related to clinical benefit and unmet need in section 1194(e)(2)) and de-emphasize manufacturer specific data elements such as cost of production and research and development costs in section 1194(e)(1)).

Furthermore, we note our serious concerns with CMS's approach regarding the collection of data on the factors outlined in section 1194(e)(1). The proposed ICR form outlines 43 pages of data requirements – the majority of which (36 pages) are related to manufacturer specific data. CMS is seeking an unwieldly amount of information for factors that have little – if any – relevance to the therapeutic value of a treatment to patients. Of additional concern, in many areas – particularly regarding research and development costs – CMS is requesting information that is simply not collected in any standardized format today. In the interest of all stakeholders, we request that CMS refocus its data submission requirements on a more limited and focused set of information. In addition, to address issues that we highlight below, we recommend that, in lieu of the proposed standardized definitions, CMS allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit on the manufacturer-specific data.

Our more detailed comments follow.

CMS must clarify how it will evaluate the evidence it receives from different stakeholders regarding the elements in section 1194(e)(2) and how such evidence will be considered in identifying therapeutic alternatives and setting the MFP.

CMS should be transparent and provide sufficient detail regarding its framework for how each piece of evidence was used to inform the identification of therapeutic alternatives for a selected drug, the establishment of the preliminary price, as well as the initial offer and response to any counteroffer, including what evidence was most impactful in CMS's analysis and why. CMS should provide a strong justification that the identified therapeutic alternatives are appropriate and primarily driven by clinical guidelines and patient need.

Furthermore, CMS's review and assessment of the evidence should be patient-centered, with a particular focus on advancing health equity and reducing disparities. To that end, we strongly support CMS's confirmation that evidence that uses discriminatory approaches such as Quality Adjusted Life Years (QALYs) will not be considered. We also note that other measures that have been often promoted as alternatives to QALYs – such as the Equal Value of Life Years Gained (evLYG) – are similarly problematic as they limit the value of interventions that both extend life and improve the quality of life – and CMS should similarly reject evidence referencing or discussing evLYGs. CMS should consider and prioritize high quality, robust real-world evidence (RWE), evidence provided by clinicians with the necessary expertise, as well as evidence submitted by manufacturers – who have a vast depth and breadth of clinical and scientific expertise regarding their marketed therapies. CMS should also focus on patient-centered outcomes, such as a patient's quality of life, and the broader societal benefit conferred by a therapy. Further, providing higher relative MFPs to products that have advanced patient care and address unmet medical need will help maintain investment in assets and clinical programs that show scientific promise.

We recommend that CMS provide manufacturers with robust detail regarding its analysis of evidence throughout the negotiation process and provide manufacturers with opportunities for discussion and dialogue, including before CMS's initial offer in February 2024 and especially in its identification of therapeutic alternatives that will be used in setting the MFP. CMS should also provide a line of sight into its assessment of the evidence for the broader stakeholder community, so as to ensure appropriate transparency and accountability not just to manufacturers but to Medicare beneficiaries and to providers and other key stakeholders.

In addition, we recommend that manufacturers should have the opportunity to review and verify third party data submissions. Manufacturers have a vast depth and breadth of clinical and scientific expertise to draw upon for their therapies, moreso than outside third parties who may make erroneous assertions in their data submissions. CMS should also confirm that third party submissions will also be done through this ICR process.

We also note that CMS's current definition of "unmet medical need" is far too narrow. In the definition for Question 43, CMS defines "unmet medical need" as a "drug or biologic that treats a disease or condition in which cases where very limited or no other treatment options exist is considered to meet an unmet medical need." [1] This narrow definition only serves to compound the harm to patients and manufacturers from this "negotiation" process. Moreover, this will only serve to continue to disincentivize further biopharmaceutical innovation, especially in these critical areas of unmet patient needs.

[1] Negotiation Data Elements ICR at 42.

We recommend that CMS look to the FDA's definition outlined in its "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.[2] Under the FDA guidance, "An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs)." The FDA's definition consists of established concepts that underpin and inform drug development and are therefore more widely understood and adopted.

CMS's Focus on Research and Development Recoupment is Misguided and Unworkable

Regarding research and development costs, a key issue for CMS must consider is that R&D recoupment for a specific therapy is a misnomer and not reflective of the way innovation occurs today. Companies invest in research and development for "programs" in a specific disease area, not simply discrete drugs or biologics. A program can have many investigational compounds or molecules at different stages of development each with multiple potential indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. This can include thousands and sometimes millions of compounds that could be screened early in the research and development process, with an overall success rate of less than 12%. Additionally, assessing therapies by primarily using research and development costs devalues therapeutic performance and harms innovation and the development of new indications and therapies.

Further, it is fundamentally mistaken to approximate "value" using research and development costs and CMS's focus on "recoupment" of these costs reflects a fundamental misunderstanding of the biopharmaceutical sector and the effort to bring new therapies to patients. Not all companies conduct research and development in the same manner. Some smaller companies might undertake single-therapeutic, high-risk approaches to developing a compound, while many others, often bigger companies, conduct research using the framework of "programs," as noted above. These differences in the way research and development is conducted could disadvantage certain smaller companies in negotiation if manufacturer-specific data is too heavily relied upon for "value."

Looking at research and development costs in the post-market setting can also be misleading because of ongoing costs that are difficult to quantify. For example, the FDA requires post-market safety monitoring for all marketed products; these costs are augmented if a manufacturer must utilize FDA-mandated risk evaluation and

[2] https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

mitigation strategies (REMS), or other post-marketing commitments or requirements, which can be costly and take years to complete.

Additionally, BIO is concerned that CMS is not consistently approaching research & development costs and revenues from an international or US basis. For example, CMS is asking for "global, total lifetime manufacturer net revenue for the selected drug" in Question 7 about research and development costs yet excluding in the instructions for research & development costs any "costs associated with receiving foreign approvals." [3] CMS should be consistent and uniformly approach the inclusion or exclusion of international revenues and expenses. Furthermore, through question 7 CMS is seemingly looking to calculate the recoupment of FDA-approved indications only, which would only be a US-based metric, by comparing them to global lifetime net revenues. This is an asymmetrical approach and focusing only on FDA approved indications also fails to capture label-enhancing research, such as different dosing regimens, new routes of administration, new delivery devices or other label enhancements that improve the patient experience.

These concerns are heightened by the fact that approximately a quarter of the questions on the proposed data elements collection form are asking specifically about research and development costs. There is little utility in requiring research and development costs to be reported to in multiple different categories which do not align with the way data are collected and reported in the normal course of business. This in turn increases the burden on manufacturers, which is further exacerbated given the extreme time constraints. We believe CMS's approach is misguided and should be reconsidered, looking at potential alternatives such as reducing the number of metrics and making them more harmonious with the way that data is collected in the normal course of business. Further, for the manufacturer-submitted data elements, including information on research and development costs, CMS should allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit.

Since each manufacturer tracks and manages R&D spending differently another approach for CMS to consider would be to amend the ICR to align with the single global figure for R&D costs such as from Securities and Exchange Commission (SEC) Form 10K filings and a simple attestation of whether or not a company has recouped the cost of R&D. If a manufacturer has not yet recouped R&D costs CMS should provide a field for the manufacturer to explain why the costs were not recouped.

[3] Negotiation Data Elements ICR at 12.

CMS Should Streamline Its Data Requirements, Focus on Existing Data Sources versus Creating New Metrics, and Clarify Definitions

There are many areas where CMS proposes to collect information that is not collected today – One example is net revenue "without patient assistance programs." It is unclear why CMS would be collecting data in this manner and the underlying implication of patient assistance programs on price. Moreover, it is unclear what CMS means by "patient assistance" as the Agency refers to it in several different contexts. One example is in Question 33, where CMS refers to patient assistance in a Part D context, disregarding the fact that manufacturers do not provide cost-sharing assistance to patients there. CMS should eliminate all mentions of "patient assistance" from its questions and from the negotiation process.

There are also other areas where CMS's rationale for asking a particular question is unclear. For example, in Question 21, CMS asks about the 340B ceiling price. [4] From the instructions, it appears that CMS will be comparing the information the manufacturer submits with what HRSA has on file. This appears to be a duplicative reporting requirement, with no good rationale for inclusion in the form, especially if CMS will already be checking this information. Ultimately, this question, as well as Question 22 asking about the Prime Vendor Program price data, are irrelevant to the overall MFP calculation and should not be included in the form as they have no bearing on the negotiation process.

In requesting certain metrics, CMS is asking for the creation of completely new pricing metrics that have not yet been defined, such as "commercial average net price" and "Part D plan best price." These metrics are unnecessary and will add to the reporting burden on manufacturers. Moreover, they will likely yield imprecise or inconsistent data across manufacturers' submissions given that these new, unestablished metrics are not well defined.

In addition, in questions such as Question 41, the extent of the data CMS is requesting is unclear. Question 41 asks about therapeutic impact and comparative effectiveness, but the instructions are unclear if manufacturers have to submit data for every indication or if they can submit on the most relevant and commonly used indications. Additionally, this is a question that would benefit from a process where manufacturers are able to submit supplemental data, especially if CMS continues to insist upon word count limits.

Moreover, there is a functional concern regarding the data requested of manufacturers in the ICR. There are some cases where manufacturers will not be

[4] Negotiation Data Elements ICR Supplemental Statement at 7.

able to comprehensively compile answers to some of the historical data points requested in the questionnaire (especially as it relates to research and development costs), as some products may have been discovered several decades ago. This creates a difficulty in providing the data that CMS requests, as the march of time could have resulted in data loss as accounting systems changed, personnel with sufficient knowledge have since been long retired, or data may not be available in the corporate archives with the level of granularity required by CMS, to name a few key concerns.

In other areas, the definitions CMS proposes are unclear, which will make it difficult for manufacturers to comply with submission requirements. For instance, "Primary Manufacturers" have no insight into patents that are not theirs, making it both impractical and legally challenging. As well, the FDA does not release information on pending patents. For another example, regarding data on approved and pending patents, clarifications are required to better define the patents and pending patent applications that must be disclosed. More precision is required where CMS is asking for patents "relating" or "linked to" the selected drug, as it is unclear what CMS means – related or linked how? In this respect, we also note that "patent" and "patent application" are well-understood terms of art that don't require further definition in the CMS guidance. For example, the CMS guidance definition of a "pending patent application" specifies any patent application "for which a patent number has not been issued." This definition would plainly include applications that are not, in fact, pending because they have been abandoned. An "approved patent application" presumably means a patent application that has received a notice of allowance, meaning that it is still a pending patent application (and not a "patent") that does not require a special definition. And a "patent" comes into existence not on the date a patent application is "approved," but on the date a patent is issued, and the official patent grant is transmitted. We recommend deleting the special definitions of "pending patent application," "approved patent application," and "expired patent," and to change the operative language as suggested in our proposed edits below.[5]

> *Patents, Exclusivities, and Approvals*
>
> *For the purposes of describing patents, exclusivities, and approvals to be collected for use in the Negotiation Program for the selected drug, as described in section 1194€(1) of the Act and section 50.1 of this memorandum, CMS intends to adopt the definitions described in this subsection.*

[5] Note that the nomenclature of "Primary Manufacturer" is retained in the edits we suggest but we note our comments later in this section that raise concerns with the "Primary Manufacturer" and "Secondary Manufacturer" construct.

- *CMS considers patents relevant to this data to include:*

    - *all patent applications pending in the USPTO, international patent applications filed under the Patent Cooperation Treaty that designate the United States, and all U.S. patents, that are owned by, licensed to, or controlled ~~pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired~~ by the Primary Manufacturer ~~relating to the~~, and that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug as of September 1, 2023;*

    - *U.S. patents ~~linked to~~ that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug where the Primary Manufacturer is not listed as the assignee/applicant but with respect to which the manufacturer has enforcement rights (for example, for a joint venture product); and any patent that is with respect to the selected drug included in a list published under section 351(k)(9) of the Public Health Service Act or section §505(j)(7) of the Federal Food, Drug, and Cosmetic Act, ~~patent applications, pending and approved~~, for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug ~~in any form~~.*

With just thirty days to work across the entirety of the manufacturer to prepare data for submission to CMS, this is a burdensome timeline to ensure a complete and comprehensive response to the numerous questions in the form, especially when there are artificial constraints on manufacturers on what they can submit, hamstringing them even further. Both CMS and the manufacturers would benefit from a streamlining of the form and reducing the number of questions asked, especially for those that are duplicative of data that CMS already have. For items such as price reporting templates, it would behoove CMS to use what they already have on hand and not create new ones for the purpose of this submission form.

Manufacturers Should Be Able to Supplement Their Timely Submissions if New Data Arises (Or Other Good Cause)

Inevitably, there will be situations where information relevant to the negotiation arises after the submission deadline has passed. Such late-breaking developments will often be completely unforeseeable at the time of submission but highly relevant

to the setting of the MFP. The potential scenarios are virtually limitless: For example, new therapeutic alternatives may come to market; production costs may shift due to ingredient shortages or supply chain issues; or new comparative effectiveness studies may become available.

The thirty-day data submission period is already an onerous requirement for manufacturers, especially with the number of questions and data that they must answer and submit. It is therefore highly possible that additional, relevant data will become available after this short timeline to submit. This ICR on Negotiation Data Elements does not outline any way in which manufacturers would be able to submit additional information after the deadline.

CMS should not blind itself to highly pertinent new information, simply because the submission deadline has passed. In the initial negotiation guidance, the Agency proposed to limit the presentation of such information to the negotiation meetings during the period after the rejection of a counteroffer. Because such information can equally inform an initial offer, the Agency should more generally permit the manufacturer the option to supplement its timely submission wherever there is good cause to do so, including when new information relevant to the negotiation process becomes available after the submission deadline.

CMS should establish a procedure that would allow manufacturers (and other stakeholders) the option to submit pertinent new information even after the deadline should the need arise. The current uncertainty for manufacturers on their ability to submit pertinent supplemental information in advance of potential negotiation meetings is another way in which the "negotiation" process has proven to be anything but fair and predictable.

Permitting supplemental submissions is well warranted. Under the statute, manufacturers are given only one month from publication of the selected drug list to prepare a voluminous submission of complex information, including information regarding Non-Federal average manufacturer price (Non-FAMP); research and development costs; production and distribution costs; federal financial support for discovery and development; pending and approved patent applications, FDA exclusivities, NDAs or BLAs and approvals thereof, market data; and revenue and sales volume data. In some cases, requested data may also not exist in a format required by CMS, such that the manufacturer will need to painstakingly convert raw data from multiple sources into such a format. CMS should require less data to be submitted, and instead rely as much as possible on existing data sources. Currently, CMS is relying on new metrics that need to be reported, such as the US commercial average net unit price, and not data that manufacturers already have access to in the course of normal business.

Manufacturers will assuredly work with utmost diligence to comply with CMS's submission requirements. Still, they may need the flexibility of a supplement to their timely submission for legitimate reasons. Ultimately, more generally permitting the manufacturer to supplement its timely submission where there is good cause would help ensure that the MFP is set based on the best available information.

Remove Limits on the Ability of Manufacturers to Respond

We are concerned that CMS's approach in this data collection form may be too limiting in practice and will not allow for a robust submission of information - including any supplementary material – by manufacturers. In particular, we are concerned with the data fields outlined in the proposed questions, which have word counts ranging from 100 words to 3,000 words. Manufacturers should be able to submit as much information as possible that is necessary for them to make an argument that they believe will be comprehensive and not limited to artificial constraints. Further, CMS also caps the number of citations allowed for certain questions at 50 citations. It may very well be the case that manufacturers will have more than 50 citations of pertinent and essential information and we ask that CMS also remove this limit as well. Moreover, the data fields do not seem to contemplate submission of complementary, non-text information within the ICR, such as charts and tables.

We strongly recommend that CMS reconsider its approach and permit manufacturers to submit any information they determine relevant to the negotiation process (including information not related to the negotiation factors enumerated in the statute). CMS should consider all such information submitted by a manufacturer, not just the negotiation factors in sections 1194(e)(1) and 1194(e)(2). Removing these limits will allow for manufacturers to adequately respond and provide apposite supporting information that can help inform CMS's decision making.

CMS Underestimates the Amount of Time It Will Take for Manufacturers to Complete Submission of the Form

In the Supporting Statement attached to the ICR, CMS provides its estimate of the burden for collecting information for the 10 selected drugs for IPAY 2026. In Section A (with table 1) attached, CMS estimates the burden to be 500 hours per Primary Manufacturer per selected drug at a base estimate cost of $51,588.50 per

manufacturer per drug. [6] We believe this estimate (and even the "high estimate CMS provides where it doubles these base numbers) are dramatic underestimates of the actual cost in time and money for each submitting manufacturer.

If selected for negotiation, this form will require manufacturers to pull different data elements from different sections of its organization for its response, as well as requesting data in some places that the manufacturer does not even have including, for example, "secondary manufacturers." Furthermore, the impact of this process and its results will have on each manufacturer means that more resources —including time and personnel—will be invested than CMS allocates for in its estimates. Moreover, the four roles or small teams that CMS outlines in its rationale for its estimate (the financial manager, cost estimator, business operations specialist, and the economist) will be just a small subset of the number of people required to submit the complete data package to CMS.

The negotiation and data submission process will be much more cumbersome for manufacturers than CMS currently estimates, and we ask CMS to reconsider these numbers.

CMS's Should Abandon Its Primary/Secondary Manufacturer Construct

We are concerned with CMS's proposal to hold a Primary Manufacturer responsible for submitting applicable information concerning a Secondary Manufacturer. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act, including to share such information. It would be fundamentally unfair and legally problematic for CMS to threaten a Primary Manufacturer with significant civil monetary penalties (CMPs) for failure to do the impossible. We note that this same concern pervades the Initial Guidance, given the numerous contexts in which CMS proposes to hold a Primary Manufacturer responsible for the action or inaction of a Secondary Manufacturer.

More Specification is Needed on CMS's Safeguards for Confidential and Sensitive Information

BIO acknowledges CMS's stated commitment to confidentiality, but recommends that CMS establish more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to

[6] Negotiation Data Elements ICR Supplemental Statement at 10.

CMS as part of the negotiation process. In addition, BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers.

BIO recommends the following minimum controls and safeguards to give full meaning to the confidentiality requirement:

> First, CMS should confirm that, in "implement[ing] a confidentiality policy that is consistent with existing requirements for protecting proprietary information,"[7] it will ensure protections comparable to, not only those under FOIA, but also those under government price reporting law and policy.
>
> We appreciate CMS's confirmation that the protections under FOIA, including the prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure,[8] will apply to information to be submitted under the program.[9] We seek confirmation that the protections under government price reporting law and policy will also apply.
>
> Second, CMS should implement robust storage and access controls and safeguards to protect the confidentiality of sensitive information. Confidentiality requirements are only as meaningful as the data privacy and security protections that are implemented to safeguard sensitive information against inadvertent or malicious[10] improper disclosure. Accordingly, CMS should implement robust systems and protocols, including by ensuring that all proprietary information stored in the Health Plan Management System (HPMS) and in electronic communications with the Agency is secure and accessible only to CMS staff and only where there is a legitimate programmatic need for access to such information.
>
> In doing so, CMS should look to the safeguards it has already established under MDRP. Under MDRP, CMS has implemented a system with numerous privacy and security protections to safeguard sensitive product and pricing data submitted by manufacturers. For example, the online interface allows a manufacturer to view its pricing data, such as its Baseline Average Manufacturer Price (AMP) data, while disallowing states, which do not have a programmatic need to view such information, from doing likewise.[11] CMS

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[7] Initial Guidance at 29.
[8] *See* 45 C.F.R. §§ 5.41, 5.42.
[9] Initial Guidance at 29.
[10] Malicious third-party cyber activities have increasingly targeted the federal government—in, part, because its databases are repositories of significant amounts of sensitive information. *Cf.* David E. Sanger, *Russian Hackers Broke into Federal Agencies, U.S. Officials Suspect*, N.Y. Times, https://www.nytimes.com/2020/12/13/us/politics/russian-hackers-us-government-treasury-commerce.html (last updated May 10, 2021).
[11] CMS, *Medicaid Drug Programs User Manual* 1 (Nov. 3, 2021).

should ensure that similar controls are in place with respect to HPMS, given CMS's intent to transition most information submissions to that system.

CMS should also specify how it will maintain the confidentiality of the subset of information that is required to be submitted via e-mail or Box. With respect to e-mail, CMS should explain, among other things, how it will enforce access security controls. In addition, we find it troublesome that CMS requests companies email data in the event that its HPMS submission system is delayed. More information is needed about this proposed backup plan, especially in the potential event that it becomes the primary submission method for manufacturers' highly sensitive data. It is important that CMS clarifies that information collected through email (in the event of the HPMS module not being completed in time) is similarly "privileged, private to the extent permitted by law, and protected from disclosure," and protected by FOIA [12] as CMS outlines that information submitted through HPMS will be. With regard to Box (a third-party commercial platform), BIO asks CMS to specify how submitted information will be kept confidential, including as against misuse by Box personnel.

***

We thank you for the opportunity to register our thoughts and concerns on this topic and look forward to future discussions. Please do not hesitate to contact us with any questions at (202) 962-9200.

xxxxx

Crystal Kuntz

Senior Vice President,

Healthcare Policy and Research

[12] Negotiation Data Elements ICR at 29.

May 22, 2023

VIA ELECTRONIC FILING - WWW.REGULATIONS.GOV

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)

Dear Administrator Seshamani:

Boehringer Ingelheim Pharmaceuticals, Inc. (BI) welcomes the opportunity to submit comments in response to the Centers for Medicare & Medicaid Services' (CMS or the Agency) Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (ICR or the ICR), including the Federal Register Notice, ICR Form (CMS-10847, OMB, 0938-NEW), and Supporting Statement – Part A. BI adopts and incorporates by reference the comments submitted on the documents by the Pharmaceutical Research and Manufacturers of America (PhRMA).

Thank you for considering these comments and those submitted by PhRMA. If you require any additional information or have questions, please contact Michael Penn, Head of Public Policy at (203)791-6680 or michael.penn@boehringer-ingelheim.com.

Sincerely,

Bridget Walsh
Vice President
Government Affairs & Public Policy
Boehringer Ingelheim Pharmaceuticals, Inc.

Christine Marsh
Senior Vice President
Market Access
Boehringer Ingelheim Pharmaceuticals, Inc.

Bristol Myers Squibb™

VIA ELECTRONIC DELIVERY

May 22, 2023

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator, Director of the Center for Medicare
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

Re: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)

Dear Dr. Seshamani,

Bristol Myers Squibb (BMS) appreciates the opportunity to comment on the Centers for Medicare & Medicaid Services (CMS) *Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)* ("Negotiation Data Elements ICR" or "ICR").[1]

At BMS, we are inspired by a single vision—transforming patients' lives through science. We are in the business of breakthroughs—the kind that transform patients' lives through lifesaving, innovative medicines. Our talented employees come to work every day dedicated to the mission of discovering, developing, and delivering innovative medicines that help patients prevail over serious diseases. We combine the agility of a biotech with the reach and resources of an established pharmaceutical company to create a global leading biopharma company. In oncology, hematology, immunology, and cardiovascular disease—with one of the most diverse and promising pipelines in the industry—we focus on innovations that drive meaningful change.

BMS supports Medicare policies that promote beneficiary access to new and effective medical treatments and help ensure Medicare patients benefit from the innovation that defines the U.S. health care system. That is why we do not support the Medicare "negotiation" and price setting policies contained in the *Inflation Reduction Act (IRA)*. We are extremely concerned by the impact that these policies will have on clinical research and future innovation for patients. BMS believes that, in the absence of full repeal of the IRA's drug pricing provisions, significant clarity and reforms are necessary in several critical areas.

The IRA will have vast ramifications for patients, providers, manufacturers, and other stakeholders across the country. BMS is concerned that misinformed, misguided, or unlawful implementation could have sweeping negative

[1] 88 Fed. Reg. 16,983 (March 21, 2023); CMS, "Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)," *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847.

repercussions with respect to Medicare beneficiary access to needed medicines, and, indeed, for *all* patients. It is vital for CMS to make every effort to maximize transparency and fairness, including meaningful consideration of and response to stakeholder feedback on its proposals, and staying within the bounds of statutory and constitutional requirements.

BMS believes that it is essential for CMS to develop and finalize a process that is open and transparent, so that stakeholders can reasonably predict how price setting will operate in practice. Any "negotiation" under the IRA should include meaningful engagement with opportunity for real dialogue, which can only occur through full transparency regarding stakeholders' comments and CMS' interpretation and evaluation of such comments. BMS urges CMS to commit to a process of meaningful engagement with opportunity for real dialogue, without arbitrary limitation on the scope of such dialogue (*e.g.*, through limitation of meetings and/or limitations on dossier submission length). Not only is such commitment necessary to effectuate Congress's intent, but it will also promote greater transparency and information sharing. We also believe it will be readily manageable for the Agency, given the limited number of drugs subject to negotiation in any given year.

BMS appreciates the opportunity to provide the following comments on the Negotiation Data Elements ICR. As with our comments to the recently released Medicare "Negotiation" Guidance,[2] we intend our input to help CMS improve transparency and clarity of the IRA's price setting program. Our recommendations reflect and are driven by our deep expertise in pharmaceutical innovation and global value assessment processes, and we offer them to help mitigate against the unintended and negative consequences the Guidance and ICR would have on innovation and, most importantly, patients.

BMS notes that a single ICR is not an adequate mechanism for providing public input and dialogue on the important process of determining the wide range of data and metrics that CMS will use in MFP-decision making. Furthermore, the proposed data submission contained within the ICR is not sufficient to address the full value of a selected medicine. We strongly urge CMS to consider the collection of information tied to both the statutory factors set forth in the IRA and data elements necessary in determining the MFP. We also ask the Agency to provide the maximum level of flexibility and transparency for said factors and elements, particularly for the Initial Price Applicability Years (IPAYs).

Key comments include:

- **Scope and Burden of Information:** BMS is concerned with both the scope and burden of information CMS will require. Manufacturers will have exceedingly short timeframes for completing and submitting the dossier (at most, 31 days from the date of selection on September 1, 2023, and the submission date on October 2, 2023). Many of the requested data, such as government price reporting information, are already available to CMS, while others are publicly available, creating additional and unnecessary burden on manufacturers. It is also not clear what CMS' legitimate need is for pricing metrics beyond non-FAMP, which is the only pricing metric explicitly listed in the IRA statute, and those that approximate the Medicare market (as this is a Medicare pricing scheme only). Even for the appropriate data elements that manufacturers *can* provide, the breadth of information coupled with the strict timelines will make the burden exceptionally high and the dossier perhaps impossible to complete and submit on time. Moreover, there may be information to which manufacturers do not reasonably have access or cannot provide with reasonable efforts. We urge CMS to critically consider which data elements are actually necessary for determining the MFP and compile said elements in the least burdensome way.

[2] CMS, "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments" (March 15, 2023), *available at* https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.

- **Global vs. U.S. Sales and Costs Metrics:** CMS alternates between requiring manufacturers to report global and U.S. sales information. BMS strongly urges CMS to *only* consider U.S.-based sales information, as Medicare prices are specific to the US.
- **Value Assessment and Evidence About Alternative Treatments:**
    - General Process: While we are encouraged that CMS acknowledges a broad and holistic assessment of value in the Medicare Negotiation Guidance, we are deeply concerned with the significantly limited opportunity proposed for manufacturers to share evidence about alternative treatments. In developing a process for value assessment in the U.S., it is important for CMS to recognize that experienced health technology assessment (HTA) markets extend greater flexibilities related to in-market value assessments, such as unlimited word counts on dossiers, transparency in the decision-making process, and more opportunities for an information exchange. Other countries have adopted a more collaborative approach with manufacturers and have implemented key procedural elements, such as structured scoping phases, indication-specific assessments, traceability of outcomes, and structured patient involvement to promote a cooperative process. As it stands, CMS' proposal does not demonstrate fluidity in these areas where other markets, with longstanding value assessment experience, do offer these cooperative procedural elements.
    - Stakeholder Input: We believe it is critical for CMS to consider a variety of perspectives throughout the value assessment process. As such, we encourage CMS to consider an appropriate forum and method for different stakeholders to provide input, rather than using a single submission format for all stakeholders. If CMS attempts to use a single set of questions to collect feedback from a variety of stakeholders, we urge the Agency to provide transparency and explicit rationale for decision making. Moreover, BMS recommends the Agency adopt a structured and transparent consultation process where relevant stakeholders are permitted to provide input in a format most suited to their expertise.

General Instructions

- "Primary Manufacturers": The Medicare Negotiation Guidance introduced the concept of "Primary Manufacturers" and "Secondary Manufacturers." The Negotiation Data Elements ICR affirms such terms, noting that the Primary Manufacturer is "responsible for aggregating and reporting all necessary data on its selected drug(s) from other parties, as applicable."[3] BMS does not agree with this approach, which is found nowhere in the statute and, at the very least, could not be imposed without proper rulemaking procedures. Primary Manufacturers may not have the legal authority to obtain such information from Secondary Manufacturers, as CMS has recognized in other contexts. And Primary Manufacturers have no ability to attest to, nor would it be appropriate for them to opine on, the data of another manufacturer. It is also impractical and unnecessary. **CMS should not require manufacturers to report information that is practically and legally unavailable to them.**

- Confidentiality of Submitted Information: BMS appreciates CMS' discussion of confidentiality in the Medicare Negotiation Guidance, and we wish to reiterate our comments related to the ICR submission. While not explicitly discussed in the ICR, we agree with CMS that the Agency should ensure confidential commercial information submitted by manufacturers during the negotiation process is protected from disclosure. We believe it is imperative that CMS ensure adequate safeguards to protect manufacturers' trade secret, proprietary, and other confidential commercial information from disclosure, including the opportunity for manufacturers to receive notice of potential disclosure and the opportunity to object to such disclosure. One suggestion to aid in facilitating the identification of proprietary information, which is utilized by certain states for

[3] Negotiation Data Elements at 2.

price transparency reporting, is for CMS to allow manufacturers to proactively designate which data are confidential and proprietary, and therefore not subject to public disclosure. BMS also asks CMS to carefully consider how the Agency intends to keep such information confidential within the Agency itself. CMS notes that manufacturers will submit the data dossier via the Health Plan Management System (HPMS) but does not detail the safeguards for ensuring data security and confidentiality. Additionally, CMS states that if the online tool is delayed, responses to the ICR will be due by e-mail at IRARebateandNegotiation@cms.hhs.gov.[4] It is unclear if the data security of CMS' email system is adequate to protect the transmission of highly confidential data. If CMS is unable to utilize HPMS for submissions, **we strongly urge CMS to more thoughtfully and thoroughly evaluate how the Agency will maintain confidentiality of proprietary information.**

- Instructions for Reporting Monetary Amounts: CMS instructs that when calculating monetary values, manufacturers should assume at most an 8.1 percent annual cost of capital.[5] BMS is concerned that the Agency inadequately considers a manufacturer's capital costs, and the cap on that cost appears to be arbitrary and uninformed. This approach further penalizes manufacturers as CMS does not seem to allow for any adjustments in future interest or inflation rate changes. In fact, in the "Research and Development in the Pharmaceutical Industry" report, in which CMS cites as supporting rationale in this ICR, the Congressional Budget Office (CBO) notes that research and development (R&D) costs "have increased by about *8.5 percent* per year over roughly the past decade."[6] In addition, when adjusted for inflation, pharmaceutical industry spend on R&D has increased over 10 times since the 1980s.[7] Therefore, CMS should apply flexibility in its approach and remove the cap on the cost of capital or, at a minimum, allow manufacturers to adjust that cap appropriately based on interest and inflation rate levels in any given year.

Selected Drug Information

This portion of the ICR necessarily presumes a mutually understood scope of a selected drug. In the Medicare Negotiation Guidance, CMS chose to issue Section 30, Identification of Selected Drugs for Initial Price Applicability Year 2026, as "final." BMS opposes this decision for several reasons, as noted in our comment letter regarding that Guidance. For example, despite not yet making any determinations of qualifying single source drugs (QSSDs), which will occur with the first published QSSD selections, CMS seeks to redefine what qualifies as a QSSD in a way that disregards statutory commands. The Medicare Negotiation Guidance also seeks to impose new substantive obligations without undertaking notice-and-comment rulemaking required by due process. Even beyond those critical legal concerns, given the importance of product scope for eventual selection and price setting, as well as the downstream negative implications to innovation and patient access for years beyond 2026, we urge CMS to meaningfully consider, and respond to, stakeholder feedback on these important topics. If CMS would have opened Section 30 for public input, for instance, BMS and other stakeholders would have been in the position to provide comment on critical issues related to IRA implementation.

It is essential for CMS to promote and allow for full transparency and input on IRA implementation; any other approach is disappointing, inappropriate, and unlawful, as CMS is using the Guidance to impose new substantive requirements on manufacturers and otherwise go beyond the statute and constitutional requirements. The Agency must seek public

[4] CMS, "Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW), Supporting Statement – Part A," *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847.
[5] Negotiation Data Elements at 3.
[6] Congressional Budget Office (CBO), "Research and Development in the Pharmaceutical Industry" (April 2021), p. 16 (emphasis added), *available at* https://www.cbo.gov/publication/57126#footnote-055.
[7] *Id*. at 5.

input on a matter of such public impact and importance, and where private rights are at stake. There is also an overriding constitutional requirement for robust and meaningful engagement on CMS' proposals regarding fundamental issues that have been apparent since the IRA's enactment in August 2022. However, because the Agency has not sought comment on Section 30 of the Medicare Negotiation Guidance, stakeholders have been deprived of the opportunity to highlight such numerous concerns. We therefore reiterate our objections stated in our comment to the Medicare Negotiation Guidance.

Research & Development Costs and Recoupment

Although the Guidance enumerates various manufacturer specific data elements that CMS "must consider," the Agency does not address with specificity how these factors will be considered to establish the MFP or adjust the preliminary price. BMS is highly concerned that the data elements that CMS has proposed to establish the MFP do not adequately capture the value and benefit of a drug to patients and the broader health care system. CMS should balance these factors such that the Agency prioritizes rewarding innovation and preserving advancements in patient care. In contrast, placing a greater emphasis on R&D recoupment, as the Agency proposes to do, is a flawed approach that ignores certain biopharmaceutical realities—such as the high risk-reward of pharmaceutical innovation and the wide range of costs incurred beyond R&D. To contextualize this broader investment, CMS should also consider historical costs tied to production, selling, and general and administrative expenses, as these metrics aid in providing a more complete picture of the drug development and commercialization process. Additionally, ongoing drug development and discovery is reliant on the commercial success of a minority of medications, compounded by the extremely low drug development success rate across all therapeutic areas, measuring at less than 7% in 2022.[8] It is important to note that no other HTA process in the world includes supply side factors (R&D costs, public funding) to determine the value of a product and/or to inform price considerations. **BMS strongly urges CMS to place a lesser emphasis on R&D recoupment, and more emphasis on the selected drug's therapeutic and clinical attributes which is the true measure of innovation.**

We encourage CMS to establish a more thoughtful, forward-looking framework (*i.e.,* not retrospective) and tie reporting to the nearest month or quarterly cutoff in the future as we believe it is impossible for manufacturers to comply with reporting dates selected arbitrarily by CMS. We are concerned that if CMS were to use an arbitrary look-back period, it could disadvantage and unfairly penalize manufacturers for previous pricing practices and data collection before the law went into effect. Manufacturers also need time to establish systems to collect this information. At a minimum, until CMS establishes this thoughtful, forward-looking frame, the Agency should set all MFPs at the ceiling price for selected drugs.

In particular, BMS seeks clarification and further understanding of CMS' intent to use global net revenues for a selected product, and we note that in other sections of the ICR, CMS looks only to U.S.-related information. **BMS strongly urges CMS to *only* consider U.S.-based information, as Medicare prices are U.S. specific. At a minimum, we urge CMS to be consistent with the sales information manufacturers must provide and then evaluate costs appropriately to that metric and market.**

Our specific comments on the "Research & Development Costs and Recoupment" elements follow.

- Basic Pre-Clinical Research for All Approved Indications of the Selected Drug: As we noted in Appendix C of our Medicare Negotiation Guidance comments, we believe that the Agency has not communicated a data request that considers a full and complete perspective of pharmaceutical development and has instead identified irrelevant and inappropriate factors for consideration. Compiling and calculating R&D costs for a drug that has

[8] IQVIA, Pipeline Intelligence (Dec. 2022).; IQVIA Institute, "The Global Use of Medicines 2023" (Jan. 2023), *available at* https://www.iqvia.com/insights/the-iqvia-institute/reports/the-global-use-of-medicines-2023.

been on the market for over a decade is a complicated process that is not easily reduced to a finite set of specific considerations, factors, or other items. We note that it is inappropriate to create a framework that not only considers historical or lifetime data reflective of early research but also assumes that the manufacturer can access information that was not required to be captured and reported. Furthermore, requesting manufacturers to retrospectively collect asset-level pre-clinical data is not feasible. We urge CMS to consider a more precise method: the Agency should invest the time in establishing forward-looking reporting requirements that start on a future date. We request that CMS utilize an individual calendar year as a starting point for all manufacturers' selected drug information.

- Post-IND Costs for All Approved Indications of the Selected Drug: BMS seeks clarification on the data elements that would satisfy CMS' inquiry on costs associated with "preparing the selected drug for clinical trials."[9] Additional context is needed to determine if this requirement refers to manufacturing costs or costs associated with the drug development process, as CMS' request is vague. CMS repeatedly refers to "personnel" in Question 2 and elsewhere in the Negation Data Elements ICR. BMS requests that CMS define "personnel" and explicitly consider both the internal and external function service providers that support and are directly associated with the study. It is vital that CMS assess these costs in totality when determining the initial MFP price and consider all direct and indirect costs that the manufacturer incurs throughout the life cycle of the selected drug.

- Costs of All Completed, FDA-Required Phase IV Studies for the Selected Drug: BMS is concerned that CMS continues to demonstrate a lack of full understanding of pharmaceutical development and research. There are different types of clinical trials conducted post-Food and Drug Administration (FDA) approval, and CMS needs to account for these factors.

- Costs of All Post-Marketing Trials for the Selected Drug: CMS needs to clarify the scope of post-marketing trials and specifically state that the Agency will include investigator sponsored studies (ISR) and real-world data gathering. Typically, these are under the purview of medical generation evidence, also referred to as "post-marketing trials," and BMS encourages CMS to further clarify its intent. Additionally, CMS must recognize and consider scenarios in which the manufacturer does not operate the study. BMS also asks CMS to provide guidance on how the Agency will consider alliances or co-development arrangements, and subsequently, how it intends for the manufacturer to consider this for reporting purposes.

  BMS notes that CMS does not appear to fully recognize the additional costs directly associated with running clinical trials, and BMS urges CMS to explicitly identify and consider these costs, specifically the purchase of third-party assets such as combination or comparator assets. BMS urges CMS to recognize and consider ongoing expenses post approval; for certain therapeutic areas, often oncology and hematology, there are costs related to continued follow-up and data generation. CMS must recognize this ongoing investment and the value of these products. Another factor that CMS should consider is the promotional costs of educating physicians on the benefit of the product.

- Costs of Failed or Abandoned Products Related to the Selected Drug: BMS strongly asserts that *all* clinicals trials conducted by the manufacturer need to be considered by CMS, not only those that were approved. "Failed" clinical trials require significant capital from manufacturers and frequently contribute to new discoveries—simply because a trial did not have a successful readout does not mean that the manufacturer did not incur expenses to develop the asset or make important scientific discoveries along the way. Manufacturers will also

[9] Negotiation Data Elements at 9.

incur a tremendous financial burden for reporting the overwhelming number of molecules and targets that do not proceed to Phase I or IND. BMS urges CMS to consider the totality of the investment, including failed and approved clinical trials.

- Costs of Other Research and Development for the Selected Drug Not Accounted for Above: BMS requests CMS to explicitly define "other research and development" costs.[10]

- Global, Total Lifetime Manufacturer Net Revenue for the Selected Drug: BMS strongly opposes CMS' intent to use global, total lifetime manufacturer net revenue for the selected drug. This requirement would include net sales information from countries outside of the U.S. and would have no place in price negotiation that is specifically based on a U.S. policy change intended for the U.S. market—and even then, is intended for the Medicare market *only*, which is only a subset of the U.S. market. While CMS notes it only intends to include R&D costs for FDA-approved indications, which is a U.S. cost and regulatory metric, the Agency seems to be calculating the "recoupment" of these U.S. costs by comparing them to global total lifetime net revenues, thereby violating a matching principle of expenses incurred and revenues earned, which will likely unfairly disadvantage manufacturers. In addition, the total net revenues earned in countries outside of the U.S. are already subject to manufacturer-payer agreements. Inclusion of those agreements (by virtue of capturing global net sales) in the CMS initial offer development is a double dip that further penalizes manufacturers. If CMS is set on its approach and intends to utilize global, total lifetime manufacturer net revenue, then, at a minimum, the Agency should recognize the costs of ongoing research and significant, necessary expenditure incurred for international product launches and line extensions.

Current Unit Costs of Production and Distribution

Supplemental to BMS' concerns in response to basic pre-clinical research costs, CMS must consider removing data reporting elements for product and development costs at the asset level prior to a specific date. There may be instances (*e.g.*, prior acquisitions, divestitures, and collaborations) where the manufacturer does not possess nor have access to such information due to previous reporting and tracking guidelines.

Additionally, CMS requires the reporting of "allocated shared operating and other indirect costs (such as capitalized production facility costs, benefits, generalized and administrative costs, and overhead expenses) specific to each NDC-9 based on unit volume,"[11] but needs to also consider the other overhead expenses that are not allocated, like freight, global quality, and the supply chain organization. BMS also requests that CMS consider expenses associated with non-manufacturing facilities that contribute to the cost of developing and marketing a selected drug.

Prior Federal Financial Support

BMS believes that the only prior federal financial support that should be reported is funding that directly resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency.

[10] *Id.* at 12.
[11] *Id.* at 15.

Patents, Exclusivities, and Approvals

BMS supports protection of intellectual property (IP) rights and believes that an effective IP framework is essential for the viability of the biopharmaceutical industry and efforts to deliver innovation that addresses unmet patient needs. The discovery and development of new medicines is a long, complex, and rigorous process. BMS is concerned that CMS' proposals could contradict the framework that was intended to protect and encourage innovation, and strongly disagrees with CMS' position in the Medicare Negotiation Guidance that the Agency may adjust the MFP downward if the selected drug has patents or exclusivities that "will last for a number of years."[12] BMS believes that CMS should not set the MFP for selected drugs below the MFP ceiling price into which patent protection extends.

CMS requests that "all pending and approved patent applications, including expired and non-expired approved patents submitted, sponsored, licensed, and/or acquired the Primary Manufacturer relating to the selected drug as of September 1, 2023"[13] be submitted. CMS is also requesting information on patents "linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant" and "for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug in any form."[14] **BMS believes that any request for patent information should be limited to information that pertains to U.S patents or applications submitted, licensed, and/or acquired directly by the Primary Manufacturer that claim or cover the selected drug as it is currently used in the commercial product.** BMS requests that CMS clarify the intended meaning of "related to" and "sponsor" as the terminology seems too broad. For example, if a Primary Manufacturer provides a drug to be used by a third party in a clinical trial, and that third party files a patent application, the Primary Manufacture might not have knowledge of such patent application or any rights to it. Additionally, BMS recommends that the Agency remove "expired" approved patents as this does not pertain to the selected drug. Complying with these requirements would be burdensome and unfair for Primary Manufacturers.

The ICR requests that manufacturers list all active and pending applications and approvals for selected drugs under 505(c) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Services Act. With respect to information on pending applications, FDA has noted that it does not report on pending applications. Specifically, FDA states, "due to confidentiality rules, FDA is prohibited from releasing information on any drug under development, review or pending approval unless the information has been made public. You may contact the manufacturer directly to ask about products under development."[15] A drug manufacturer would not have insight into another sponsor's pending applications with the FDA, so this data request is operationally impractical. Additionally, FDA "will not publicly disclose the existence of an application or abbreviated application before an approval letter is sent to the applicant or tentative approval letter is sent to the applicant unless the existence of the application or abbreviated application has been previously publicly disclosed or acknowledged."[16] Given these parameters, we request that CMS remove this requirement. In addition, to limit manufacturer burden, we urge CMS to utilize FDA's publicly available resources (*e.g.,* Orange Book, Purple Book, and Drugs@FDA) to procure patent information.

[12] *Id*. at 53.
[13] *Id.* at 19.
[14] *Id*. at 20.
[15] FDA, "Frequently Asked Questions about CDER," *available at* https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/frequently-asked-questions-about-cder.
[16] *See* 21 CFR Section 314.430.

Market Data, Revenue, and Sales Volume Data

BMS has serious concerns with CMS' proposals in the "Market Data, Revenue, and Sales Volume Data" section of the ICR. In compelling a manufacturer to "agree" to the disclosure of certain information, the Agency is bound by constitutional and statutory requirements, and should otherwise seek only to gather what is required for anticipated "negotiation" of the MFP. Yet the Agency appears to read "market data and revenue and sales volume data for the drug in the United States" in an exceedingly broad way. The Agency cannot, and should not, impose an obligation to divulge virtually *all* pricing information for the drug, including proprietary, otherwise reported, and irrelevant information. BMS objects to CMS' proposed information collection in this section based on appropriateness, relevance, duplication, excessive scope, and undue burden.

- Duplicative Reporting Requirements: We note that the Secretary of Health and Human Services already has access to the 340B Ceiling Price and Medicaid Best Price through existing government price reporting. Manufacturers should not be required to re-report this information to the Agency, which should have easy access to such information within its own Department. Furthermore, requiring five years' worth of data on the 340B Ceiling Price and Medicaid Best Price is unduly burdensome for a manufacturer to provide, not to mention seemingly irrelevant for determining an MFP in the *Medicare* market. We also note that Federal Supply Schedule (FSS) and Wholesale Acquisition Cost (WAC) prices are already publicly available and do not need to be re-compiled by manufacturers.

- Appropriateness and Relevance of Reporting Requirements: BMS strongly objects to CMS requesting data on pricing metrics that do not reflect an actual Medicare price and therefore have no bearing on a Medicare-negotiated price. By creating a Medicare "negotiation" scheme, Congress has directed CMS to use market data, revenue, and sales volume data to come up with a new pricing metric reflective of the Medicare market. And by referring to final FSS and Big Four prices, for example, CMS would be capturing complexities of those calculations that should not apply to IRA price setting. Reference to FSS and Big Four prices could have the unintended consequence of reducing or eliminating manufacturers' voluntary discounts that lead to lower prices for those government channels. Such pricing may be inherently short-term and thus would serve as an inappropriate benchmark for setting a longer-term price. CMS inappropriately requests utilization data, for example, 340B utilization, which is not necessary for the purpose of MFP negotiation. CMS also seeks to create new methodologies, such as multiple variations of U.S. commercial unit prices. Not only are these methodologies not relevant in determining a Medicare-based price, but they would be near impossible for manufacturers to develop and validate within a 30-day timeframe.

Consistent with our comments in other sections, BMS is also concerned with how vague CMS' phrasing of timeframes is portrayed throughout the ICR, and particularly so in the "Market Data and Revenue and Sales Volume Date" section. BMS believes that the lack of consistency, coupled with broad time ranges, could inadvertently lead to discrepancies in data reporting—and despite reasonable efforts to comply with CMS' newly-created, extremely-detailed requirements within incredibly short timeframes, manufacturers could be subject to severe civil monetary penalties (CMPs) should there be an error or miscalculation in submitting these data elements.

BMS asserts that only information germane to determining an MFP for the Medicare market should be included in the manufacturer's dossier submission (*i.e.,* commercial and/or non-Medicare government pricing information should not form the basis of a Medicare price). We question the legitimacy of CMS' request for this pricing information as it relates to the purpose of this ICR. **The IRA statute only refers to submission of manufacturer non-FAMP, and not the other pricing metrics proposed in the ICR, and BMS urges CMS to remove these extraneous reporting requirements. We also**

ask CMS to only finalize submission requirements that are essential for operationalizing the Medicare price setting process and to do so in the least burdensome way possible.

BMS agrees with CMS' approach to considering primary manufacturer acquisition costs of the selected drug and thanks the Agency for acknowledging these costs. However, those costs appear to be explicitly excluded from the definition of R&D and mentioned as a separate category in the ICR. Costs associated with one manufacturer acquiring another is a common practice of unlocking innovation and should be viewed as inseparable from total R&D costs. BMS urges CMS to evaluate R&D costs and acquisition costs together when deciding whether the selected drug recuperated its R&D costs. In addition to acquisition costs, it is also critical that CMS considers costs of in-licensing, joint ventures, co-commercialization agreements, partnerships, and other forms of acquisition as each contributes individually but significantly to a manufacturer's R&D capabilities and results in innovative medicines being delivered to patients who need them.

Evidence About Alternative Treatments

As stated in our Medicare Negotiation Comments, BMS supports CMS' intent to analyze a full body of qualitative information when reviewing the clinical benefit and encourages CMS to go beyond outcomes and safety profiles of the selected drug and therapeutic alternatives to deeply consider a robust body of information when assessing a selected drug's impact on unmet need and therapeutic advance. This holistic consideration should go beyond rigid health care costs and health outcomes to consider the impact of medicines on society—such as improvements to patients' and caregivers' lives, efficiency and quality in the health care system, and equity across populations.

We are deeply concerned with the significantly limited opportunity proposed for manufacturers to share evidence about alternative treatments and how this opportunity is arbitrary and more restrictive than traditional value dossiers. Across all questions related to "Evidence About Alternative Treatments," there is an 8,000-word limit and even less flexibility with individual word and citation limits for each of the four related questions. As response formats are proposed in the ICR, there also appears to be no ability to share evidence data in tables and graphic charts that could make it more clear for CMS to review.

In developing a process for value assessment in the U.S., it is important for CMS to recognize that experienced HTA markets with long established frameworks (*e.g.*, Germany, France, UK, Canada) extend greater flexibilities to manufacturers related to value assessments, such as unlimited word counts on dossiers, transparency in the decision-making process, and more opportunities for an information exchange. Other countries have adopted a more collaborative approach with manufacturers and have implemented key procedural elements to enhance the value assessment process, such as structured scoping phases, indication-specific assessments, traceability of outcomes, and structured patient involvement to promote a cooperative process. As it stands, CMS' proposal does not demonstrate fluidity in these areas where other markets, with longstanding value assessment experience, do offer these cooperative procedural elements.

Our specific comments on the Evidence About Alternative Treatments elements follow.

- Respondent Information & Instructions: CMS has suggested that all stakeholders, including health care providers, patients, and others, can submit evidence utilizing the same form and questions. While we believe it is critical for CMS to consider a variety of perspectives throughout the value assessment process, it is equally as important to establish a manageable and systematic process that enables the Agency to deal appropriately with the information that is submitted and more importantly to add robustness and credibility to the entire effort. To

do so, CMS must approach different stakeholders uniquely and provide an appropriate forum and method for stakeholders to deliver the information relevant to their areas of expertise. If CMS attempts to use a single set of questions to collect feedback from a variety of stakeholders, we urge the Agency to provide transparency and explicit rationale for decision making. More importantly, **BMS recommends the Agency adopt a structured consultation process where relevant stakeholders are permitted to provide input in a format most suited to their expertise.**

In the instructions, CMS indicates that evidence contributors should not include comparative effectiveness research that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value, and attempts to reinforce this requirement through a simple "yes/no" checkbox after Questions 41 - 43. While we appreciate CMS' attempt to have submitters exclude this information, we are concerned that these instructions are not clear enough, leaving ample opportunity for CMS assessors to be exposed to such metrics. We request that CMS specify that submitters do not use *any* quality-adjusted life-year (QALY)-based cost effectiveness metrics (including cost per equal value of life years gained [evLYG]) and direct submitters to put an asterisk or other indication next to the citation of any study that includes QALY-based cost effectiveness metrics. **Additionally, BMS strongly recommends that CMS not only perform its own checks and due diligence to ensure that any analyses based on QALY are excluded from review, but also allow manufacturers to validate CMS' evidence evaluations, which would provide further safeguards against discriminatory metrics being used to assess and determine value of important medicines**

While new methods like generalized cost-effectiveness analysis (CEA) are being explored to account for differential value of health improvement in different contexts, there is no consensus yet on the ability of these methods to adequately address health equity considerations for special populations. Further, CMS has not sought public comment from patients and other stakeholders on willingness to pay and appropriate cost effectiveness thresholds for IRA value assessments in general. **Therefore, BMS strongly recommends that CMS not anchor value assessments for selected drugs on CEA. Any consideration of CEA should merely be a part of a broader and holistic assessment of value.**

- Prescribing Information: CMS is seeking evidence submissions related to FDA-approved prescribing information. However, this is inconsistent with CMS' proposed approach in the Medicare Negotiation Guidance where the Agency proposed considering off-label use supported by evidence-based guidelines and CMS-approved Part D compendia when identifying indications for the selected drug and therapeutic alternatives. BMS reiterates the importance of a structured scoping process and dialogue with manufacturers to define appropriate therapeutic alternatives to ensure that manufacturers are given the opportunity to submit the appropriate evidence. If manufacturers and other stakeholders' submissions do not address potential off-label use for this question, stakeholders, particularly manufacturers, may presume that CMS will exclude that consideration from the value assessment. **Accordingly, BMS suggests that CMS follow suit with fellow HTA countries and limit evidence submission to licensed comparators only.**

- Therapeutic Impact and Comparative Effectiveness: BMS is pleased that CMS is proposing to consider an array of evidence submitted by manufacturers and the public on the selected drug and therapeutic alternatives as part of its effort to "negotiate" MFPs. However, we are deeply concerned by the stringent evidence submission limits as outlined in the ICR.

  BMS asks CMS to reconsider its proposal to ensure that any information collection process allows manufacturers to submit a comprehensive evidence package in the Academy of Managed Care Pharmacy (AMCP) dossier

format, which is a widely used, gold standard dossier submission format for value assessment purposes. Furthermore, BMS urges CMS to extend the flexibility to permit reasonable assumptions and submit additional data to account for the distinctive qualities of the treatment selected for negotiation. While we understand that CMS will be undertaking a significant exercise in reviewing data submitted by manufacturers and other stakeholders on comparative effectiveness information, we are concerned that the text data format and rigid word limits proposed will constrain the ability of manufacturers to share important evidence on the values of our medications. When submitting a dossier to the Agency, there should neither be limitations on file sizes nor transmission options. Transparently, it would be simpler and clearer to convey comparisons of health outcomes for a selected drug and therapeutic alternative(s) through tables and charts, but that format does not appear to be permitted with the proposed text format. **We urge CMS to allow for other formats and/or links to supplemental materials to provide thorough responses to CMS' questions. It will be practicably impossible to attempt to provide adequate evidence for multiple indications of a given drug within the proposed 3,000 word and 50 citation limits.**

BMS urges CMS to consider any information submitted by manufacturers, even if that information is not tied to a specific statutory factor. This approach is consistent with the plain language of the statute. Like CMS "offers," manufacturer "counteroffers" must be justifiable based on the statutorily enumerated factors. Nothing precludes manufacturers from voluntarily providing additional information to CMS that may also bear on the Agency's decision-making.[17] BMS notes that CMS has clear authority to consider all information submitted by manufacturers, whether or not tied to a statutory factor, and that the Agency should consider all information submitted by a variety of stakeholders. In addition, unlike justifications for offers or counteroffers, CMS' responses to counteroffers need not be justified by reference solely to the statutorily enumerated negotiation factors.[18]

CMS has indicated that it will conduct internal analytics as part of the evidence assessment process. BMS believes that a proper value assessment should be a collective process with transparent methods. To that end, should CMS generate real-world evidence (RWE) and/or employ modeling techniques, **BMS reiterates that it is critical for manufacturers to have the opportunity, and ample time, to review and comment on the underlying assumptions and approaches to support a good-faith, transparent value assessment.**

- Comparative Effectiveness on Specific Populations: In the Medicare Negotiation Guidance, CMS indicates that priority will be given to studies focusing on special populations (including individuals with qualifying disabilities, patients with End-Stage Renal Disease [ESRD], and Medicare-aged populations) over studies for which these populations were not the primary focus. While BMS agrees that benefits and risks to these special populations are critical to assess, depending on the size of the special population relative to the overall patient population, there may be numeric differences in outcomes for a selected drug compared to its therapeutic alternative that are not statistically significant (or may not be replicable in a similar population). We recommend that CMS consider subgroup/population analysis as a core assessment with safety and efficacy and that evidence from these studies be considered of equal priority to evidence from larger studies that are better powered to draw comparative effectiveness conclusions. **We also encourage CMS to consider evidence in other subpopulations, including patients with comorbidities and different ethnicities, when data is available, and ask that CMS require submitters to speak to the quality of evidence and/or be prepared to assess that quality during the Agency's internal review process.**

[17] *See* SSA § 1194(b)(2)(C)(ii)(II).
[18] *Compare id.* § 1194(b)(2)(B) and (C)(ii)(II) (justifications for offers and counteroffers must be based on statutorily enumerated negotiation factors), *with id.* § 1194(b)(2)(D) (no similar requirement for responses to counteroffers).

- Addressing Unmet Medical Needs: CMS intends to define unmet need as treating a disease or condition in cases where very limited or no other treatment options exist. This is an unduly restrictive definition of unmet need. As CMS will assess medications in the middle of their life cycles, BMS recommends that unmet need be considered from initial approval to the time of assessment. Additional value should be particularly considered for those medications that treat serious medical conditions, including those that make incremental steps toward curative goals. Further, unmet need should be viewed from the perspective of patients and providers. Unmet need should accordingly encompass a spectrum of characteristics, such as: alternative dosing regimens; route of administration; reduction of side effects; and shorter treatment periods.

***

BMS appreciates the opportunity to comment on the Negotiation Data Elements ICR. We would be pleased to discuss these comments in further detail. Should you have any questions or concerns, please contact Caroline Tucker, Director, Executive Branch Strategy, at caroline.tucker@bms.com.

Sincerely,

/s/

Amy Demske
Executive Director, U.S. Policy and Executive Branch
U.S. Policy & Government Affairs

Date

May 22, 2023

CareSet Comments on CMS' Negotiation Data Elements Information Collection Request (CMS-10847)

These comments are in response to the information request found here: https://www.govinfo.gov/content/pkg/FR-2023-03-21/pdf/2023-05784.pdf

Please note, below are the same comments CareSet submitted in April 2023 for the Medicare Drug Price Negotiation Program Initial Guidance, sent to IRARebateandNegotiation@cms.hhs.gov. Our previous comments also apply to this Proposed Collection Comment Request:

Under the Inflation Reduction Act (IRA), Centers for Medicare and Medicaid Services (CMS) will negotiate fair pricing for high-cost medications. CMS will also have to decide which data and evidence it receives from drug manufacturers during this negotiation process will be released to the public.

This negotiation must balance two opposing goals. First, Medicare beneficiaries deserve to pay reasonable prices for the medications they need, and second, pharmaceutical companies must be allowed to sustain profits that justify access to the financial capital they need to create new medications. This policy balance is embodied within the law with the concept of the Maximum Fair Price (MFP).

CareSet is a healthcare research and data journalism organization, as well as a data vendor. There are two general categories of interest to CareSet within this guidance.

- What information should be considered proprietary?
- What types of evidence should CMS accept when it evaluates the performance of medications?

Achieving the right balance on these issues will allow researchers, journalists, and members of the public to measure the effectiveness of the law, related regulations and guidance, and the government's performance in negotiating lower medication costs.

What information should be considered proprietary?

CMS will publish portions of the information that was submitted by the pharmaceutical company as part of the negotiation process. CMS has requested feedback regarding what information should be regarded as proprietary to avoid "treating information that does not qualify for such protection as proprietary."

CMS has also requested feedback on what components of the negotiation process itself should be private and the degree to which that privacy should be permanent.

The IRA instructs the Secretary to determine what information will be considered proprietary [42 U.S.C 1320f–2(c)].

CMS has a responsibly to demonstrate the effectiveness of its IRA implementation

The central mandate from Congress to CMS is to create "a consistent methodology and process" that achieves "the lowest maximum fair price for each selected drug".

FOIA exists to inform the public about the actions of its government and to provide citizens with political choices. It mandates the release of materials that are "likely to add to the fund of information that citizens may use in making vital political choices". Given the unprecedented nature and political controversy of the IRA, the public being informed of the success of the IRA and its implementation will likely be of great importance to FOIA courts.

CMS must not create a commitment to the industry that data will be proprietary

CMS should not embed any specific promises, in regulation, that certain information is proprietary to medication manufacturers. Doing so creates an expectation that an exemption to FOIA should apply where none is warranted and means that information might be permanently withheld from public scrutiny. It should be the responsibility of the drug manufacturers to assert what should be private and then CMS should evaluate those assertions. There is no reason for CMS to proactively protect any specific information by making promises in regulation that will be enforced even after they have become out-of-date.

FOIA Exemption 4 governs evaluation of the proprietary status of information submitted to the government.

The first component of evaluating whether information is proprietary under Exemption 4, post-*Argus*, considers whether data is "customarily kept private, or at least closely held".

The second component is whether the government provided an assurance that information would be kept confidential.

Prices should not be proprietary

The central mission of this negotiation program is to use the volume of patients covered under Medicare to negotiate a favorable rate for the purchase of medications. It is only comparison with the non-FAMP (i.e. the prices charged outside of Medicare) and Plan Specific Enrollment Weighted Amounts (i.e. prices charged within Medicare Part D) that allows for the public to be able to evaluate whether this program is working.

The CMS guidance only conceptualizes information as "proprietary" or "already public". However, this ignores the "industry arcana" effect, where an industry excludes outsiders from information, while ensuring that everyone in the industry is well-informed.

Manufacturers cannot argue that prices are kept private, when an entire industry exists that relies on perfect or near-perfect knowledge of pricing. Data vendors sell medication pricing information regularly to third parties, which is how the manufacturers know what their competitors are charging for their products.

This knowledge hardly qualifies as proprietary, since at least three parties know the price of all large payor transactions, given that prices are negotiated by Pharmacy Benefit Managers (PBMs). Therefore, multiple parties are "in" on the financial details of nearly every medication price negotiation.

However, the industry still excludes Congress, researchers, and journalists from the data they need to understand if a market is functioning correctly. Given that PBMs are now connected with both pharmacies and insurance companies, this knowledge is well-disseminated. In short, the only people who are not aware of medication industry pricing are those entities that would seek to hold the medication industry accountable for those prices. CMS should never consider information that the majority of an industry knows to be "private", and should therefore consider the wide commercial availability of data that they choose to label as "proprietary". This principle applies centrally to prices, but is also relevant to other types of information.

A rule of thumb: if a pharmaceutical manufacturer cannot demonstrate that their "confidential" data is not well-known by their competitors, then CMS should ensure that this data is fully open to the public.

To illustrate this point - If Medicare is currently paying a manufacturer $100 for a pill and the new negotiated MFP is $90, this might seem like a victory for CMS. However, if the public was aware that the going rate for the medication to other payers is $70, it would be clear that taxpayers are overpaying. Without the "going rate" information it will be impossible to tell whether CMS is actually successful in its negotiations.

If CMS is unwilling to provide this transparency, then CMS must clearly delineate the manner in which it will demonstrate to Congress and the public that its program is calculating the right price.

Process should not be entirely private

CMS asks for feedback on the currently secretive negotiation process. The process includes rounds of negotiations with evidence being passed back and forth between a manufacturer and CMS, most of which is held private until it is ultimately deleted.

We understand that at least some parts of the negotiation should be private. However, CMS should avoid policies which block transparency forever. CMS should consider methods to enable partial transparency. For instance, CMS should insist that all efficacy and cost-effectiveness research that is used by the manufacturer during the negotiation be listed publicly. CMS should publish a list of which evidence was referenced by both CMS and the manufacturer, during each step of the negotiation process, including research on medications that are in competition with the medication under negotiation.

CMS should further consider releasing the full negotiation records 5-10 years after the patent coverage for a medication expires, rather than mandating that they be destroyed.

Generally, CMS should be embracing a multi-pronged approach in protecting the vital trade secrets of manufacturers, as well as providing the marketplace with open data and evidence on whether a specific medication is worth its costs. If these suggestions are not workable, then CMS should consider other mechanisms to inform the marketplace of relevant data to ensure long-term competition to lower prices across many different medication classes and diseases.

What drug performance data should be considered as part of ongoing negotiations?

CMS will also be required to gather and evaluate evidence regarding the effectiveness of medications. CMS should accept data of various types and not only those currently in vogue for real-world evidence. This includes:

- Evidence that is not released as articles in medical journals, including alternative evidence containers such as whitepapers and data dashboards.
- Aggregated patient experiences, including those from patient data registries.

CMS evaluations of evidence (both from manufacturers and from third parties), should be fully transparent. If CMS does not think evidence is relevant, it should clearly state why for each evidence submitted. Journalists and researchers should be able to easily quantify and analyze the evidence evaluation process to determine if CMS is preferring certain types of evidence, researchers, or research approaches.

CLL SOCIETY

VIA ELECTRONIC DELIVERY

May 22, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: Information Collection Request (ICR) for Negotiation Data Elements (CMS-10847)

Dear Administrator Brooks-LaSure:

CLL Society appreciates the opportunity to submit its comments on the Centers for Medicare & Medicaid Services' (CMS') Information Collection Request (ICR) for Negotiation Data Elements toward implementation of the Drug Price Negotiation Program (DPNP) created under the Inflation Reduction Act (IRA) of 2022.

CLL Society is dedicated to addressing the unmet needs of those within the chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) community through patient education, advocacy, support, and research. Our patients live with a chronic, rare cancer of the immune system. CLL Society is the largest nonprofit focused exclusively on the unmet needs of those living with CLL and SLL.

As a patient advocacy organization, we strive to ensure that patients have access to safe and effective treatment options by informing patients and caregivers about the rapidly changing therapeutic landscape and the importance of clinical trials, supporting and building patient networks, engaging in research, and educating healthcare providers, patients, and their caregivers. We also recognize that the healthcare landscape extends beyond science, clinical care, and patient support. CLL Society is deeply concerned that while the IRA's DPNP may marginally ease financial burdens for Medicare beneficiaries with CLL/SLL, its implementation has the potential to exert a detrimental force on equitable access to existing treatments and disincentivize research and development for new and better therapeutic options.

As we noted in our comments to CMS' Initial Guidance implementing the DPNP, the decisions the Agency makes now will be incorporated into the decision processes for researchers, investors, and manufacturers as they determine whether to pursue a particular drug candidate for an indication. Similarly, any procedural hurdles to fully engage patients living with CLL/SLL, and the clinicians treating them, will reduce both the breadth and accuracy of the information upon which CMS will base its initial offer and evaluate any manufacturer counteroffer(s). Clinical trial data is an essential

component of evidence on treatment value, but it fails to capture real-world treatment outcomes as it evolves over time.

Our comments provide a brief background on CLL/SLL and focus on data elements within the context of our patient community. We will also outline our concern that the framework articulated in CMS' Initial Guidance, particularly the policy and statutory interpretation determinations on drug selection released as final guidance, increases the burden on stakeholders. These determinations also decrease the ICR's alignment with the statutory concept of determining a maximum fair price (MFP) for single-source "monopoly" drugs. CLL Society remains concerned that the MFP generated from the Initial Guidance and the ICR will be distorted by aggregation of data on alternative therapeutic options as well as unmet needs across multiple NDAs/BLAs with indications in disparate disease states and patient populations.

We continue to urge CMS to fully engage stakeholders so that its policy determinations and exercise of discretion will avoid disrupting incentives to scientific advances that have provided hope for blood cancer patients and their families.

Background

CLL is a chronic blood cancer of a type of white blood cell called the B-lymphocyte. In CLL there is a progressive accumulation of too many mature B-lymphocytes. CLL is the most common leukemia in adults in the United States, with around 18,000 cases diagnosed annually. Besides being a type of leukemia, it is also classified as a type of non-Hodgkin's Lymphoma (NHL). So CLL is both a leukemia and lymphoma at the same time. SLL is simply a different manifestation of the same disease and is best understood as a different stage of CLL where there are not a significant number of cancer cells just yet located within the bloodstream. When the cancer cells are only found in the lymph nodes it is called SLL. When the cancer is found in the bloodstream and possibly elsewhere, including the lymph nodes, it's called CLL.

CLL/SLL is extremely heterogeneous, meaning each person's disease type and the way the disease progresses can be extremely variable. Some individuals experience rapid deterioration due to having an aggressive form of the disease and survive for as little as two years, while others have a less aggressive form of the disease that may never need treatment and they can expect to have a normal life expectancy.

Targeted therapies, such as BTK inhibitors and the BCL2 inhibitor known as venetoclax, offer substantial efficacy against CLL/SLL and have transformed care for those in our community affected by this disease. Patients now have more treatment options compared to ten years ago when the standard of care was chemoimmunotherapy, which did not necessarily work on all forms of the disease. Now, they can take an oral continuous BTK inhibitor, with or without a monoclonal

antibody, until their disease progresses. Alternatively, patients can choose a shorter time-limited treatment approach that combines venetoclax (which is currently the only approved BCL-2 inhibitor) and a monoclonal antibody. The latter approach enables dose discontinuation until active monitoring reveals that the disease has again progressed to a degree that indicates a different treatment is needed.

Although most CLL/SLL patients can expect a response to initial therapy, nearly all current treatment options are palliative and not curative. Most patients will experience one or more relapses during the course of their disease. Many are forced to either adjust their dosing due to side effects, take a "drug holiday," or completely discontinue the drug due to intolerance. For patients with relapsed/refractory disease or drug intolerance, treatment decisions are highly individualized based on prior therapies, prior response, the reason for discontinuation of previous therapy, comorbidities, biomarker characteristics, patient preference, and therapeutic goals. Patients will experience serial relapses over their lifespans, and many will be treated with all available agents at some point during their disease course.

The experience with PI3K inhibitors in CLL/SLL illustrates the inherent difficulties surrounding studying treatments for this rare disease and the heightened risk that drug manufacturers take on when pursuing new therapeutic candidates. Delays in approval that are directly associated with the wait for overall survival data have already dampened research efforts for CLL/SLL and slowed patient access to potentially life-saving therapies. CLL Society has advocated for crossover in clinical trials because it saves lives, but the strategy inherently compromises the "purity" of overall survival data. Since CLL/SLL is not an ideal disease state from a research perspective, new treatments are often approved for other types of cancer and then later approved for CLL/SLL.

As more fully discussed below, CLL/SLL serves as a perfect example as to why there are several unmet needs for those whose disease progresses to the point of being in a life-threatening condition despite the availability of other FDA-approved treatment options. Similarly, existing CLL/SLL treatment options are not interchangeable alternatives for patients when they move through initial treatment, complete response, relapse, second-line treatment, complete response, relapse again, and then progression.

CMS' Initial Guidance increases the burden associated with the ICR and decreases the sufficiency and utility of the information to be collected.

CLL Society understands that CMS is charged with implementing the DPNP on a very tight timeline. Unfortunately, CMS' commitment to timely implementation deprived the Agency of the stakeholder feedback it needed to implement the DPNP, including the ICR, without undue burden on stakeholders and to derive MFPs based on the factors specified in the IRA for each selected drug. Procedural safeguards ensuring public input from impacted stakeholders, including notice and comment, are particularly critical when implementation mechanisms are driven by policy

decisions and legal interpretations that diverge from or are arguably inconsistent with, statutory language.

CLL Society reiterates its request that CMS reconsider its decision to identify a qualifying single-source drug based on common active moiety (drugs) or common active ingredient (biologics). An approach that treats products as the same qualifying single-source drug only when they share an NDA or BLA is within the plain language of the statute. It would reduce the burden on manufacturers complying with the ICR, and it would increase the utility of the collected information in identifying an MFP informed by unmet need, treatment value, and available alternative therapies. It would also eliminate the conflict between the IRA's timeline from NDA/BLA approval to negotiation eligibility and CMS' implementation of the DPNP. For our patients, however, the most important concern is that CMS' interpretation reduces the value of new indications to manufacturers and their shareholders. We understand from anecdotal reports that one or more drug manufacturers have shut down research and development efforts toward NDAs for new uses of existing drugs, due to concern that any new NDA would be subject to an MFP earlier than what was anticipated from the statutory language.

We are also concerned that CMS' implementation creates another substantial set of burdens that are not required under the statute. Although CMS' ICR states that the IRA requires and authorizes CMS to collect information from Primary Manufacturers, the law does not explicitly address situations in which more than one entity meets the definition of a manufacturer for DPNP purposes. Manufacturers often develop drug candidates and license one or more indications to a partner. Research and development costs may be split across multiple entities and a manufacturer with data on those costs may not have access to data on sales volume, revenue, and other data elements required within the ICR. CLL Society expects that more robust stakeholder engagement could have permitted CMS to avoid situations in which a primary manufacturer would be responsible for securing information in the possession of, or even confidential to, a secondary manufacturer. We expect that these scenarios create a substantial burden to manufacturers that is not captured in CMS' estimates.

Stakeholder input on alternative therapies and unmet needs is crucial to identify an appropriate MFP.

As noted above, BTK inhibitors offer considerable improvements in care for our patients but can result in drug intolerance requiring discontinuation. Zanubrutinib is a BTK inhibitor with an orphan designation and approval for the treatment of mantle cell lymphoma (2019) that has demonstrated fewer cases of atrial fibrillation than ibrutinib and no cardiac-related deaths. CLL/SLL patients taking zanubrutinib also have a higher response rate and a longer time to disease progression.

The reduced side effect profile for zanubrutinib will enable patients to remain on treatment longer, but once their disease progresses, they cannot simply switch to one of the other irreversibly

binding BTK inhibitors that are approved for CLL/SLL and expect a response. This is because once a drug within that same BTK inhibitor drug class has failed the patient, all drugs within that same class will also likely fail. All FDA-approved CLL/SLL treatments are, therefore, not a set of alternatives that can be deployed throughout a patient's disease course.

Questions 40 through 43 of the ICR are designed to enable manufacturers and the public to share information on a selected drug, therapeutic alternatives, and the extent to which it addresses an unmet need, and/or represents a treatment advance. We appreciate that CMS intends to develop a mechanism for patients and their providers to weigh in on treatments selected for negotiation. But we remain concerned that the processes for submission could deter patients, treating clinicians, and patient advocacy organizations from submitting feedback and information. CLL Society offers the recommendations below to improve the information CMS is able to obtain from public stakeholders and guide its analysis of unmet needs and therapeutic alternatives:

- CMS should solicit public input on selected treatments and any therapeutic alternatives through regulations.gov and accept comments and input through that portal or through an email address designated to accept public input within the negotiation process. Neither patients nor patient advocacy organizations are familiar with HPMS, and we are unaware of it having been used for similar purposes in the past.

- The 30-day comment period is far too short for patients, patient advocacy organizations, and clinicians to collect and provide meaningful input on selected drugs and their therapeutic alternatives. We ask that CMS provide clear notice of opportunities for stakeholder input and that it accept information from non-manufacturer stakeholders throughout the negotiation process.

- Limitations on the number of words or citations that can be submitted to CMS are unlikely to encourage stakeholder input or to increase the relevant information submitted to the Agency. We ask that CMS remove those limitations and accept public input through regulations.gov or email submission.

- CLL Society is concerned that Section J, **Certification of Submission for Respondents Who Are Not Primary Manufacturers Required for All Respondents Who Are Not Primary Manufacturers,** is identical to the certification required from manufacturers. Patients and their advocacy organizations will likely experience questions and concerns regarding any legal jeopardy associated with informing CMS about their experience with drugs selected for negotiation. The cautionary statement on potential civil or criminal liability will all but foreclose the valuable input from clinicians and researchers that could improve CMS' ability to determine an appropriate MFP.

- Non-manufacturer stakeholders must certify that the information is complete and accurate, but CMS does not provide any guidance on the difference between complete and incomplete submissions.
- Stakeholders would commit to "timely notify CMS if I become aware that any of the information submitted in this form has changed." This may apply to a researcher involved in studies for a selected drug or therapeutic alternative but does not appear applicable to the general public, patients, patient advocacy organizations, or clinicians.
- Any individual or entity electing to submit information must acknowledge that they "also understand that any misrepresentations may also give rise to liability, including under the False Claims Act." We strongly urge CMS to eliminate the certification requirement for non-manufacturer stakeholders.

- The MFP is a single price for each selected and negotiated drug under the Medicare program. The IRA negotiation process outlines considerations such as alternative therapies, unmet needs, and the extent to which a treatment represents an advance in therapeutic options.

    - The instructions preceding questions 40-43 note that declarative statements must be supported by evidence with a citation unless the information concerns personal experience prescribing or taking the drug. CLL Society, like other patient advocacy organizations, is well-positioned to communicate the needs and concerns expressed by our patient communities. We urge CMS to permit and consider patient information submitted by patient advocacy organizations.

    - Information on alternative therapies is indication-specific. CMS' decision to utilize costs of alternative therapies in calculating an initial offer does not appear reasonable unless the selected drug is defined by an NDA/BLA rather than moiety or active ingredient.

        - Due to the approval of new treatment options over the past several years, patients with CLL/SLL are now living longer. However, CLL/SLL patients often experience multiple remissions and relapses throughout their lifespan, so living longer with the disease means there is a good chance they may run out of treatment options the longer they live. All FDA-approved treatment options are not interchangeable as alternative therapies for patients as their disease progresses. Patients may be unable to tolerate an entire drug class or have multiple relapses after being treated with all available therapies.

Options are based on previous treatments, patient-specific factors potentially driving tolerance and/or effectiveness, and the aggressiveness of their disease.

- The definition of unmet medical need CMS intends to adopt for DPNP purposes is narrow. CLL Society urges CMS to acknowledge that there is an unmet need when patients are adversely impacted by a condition ***despite*** the availability or use of treatments.
    - For CLL/SLL patients, the unfortunate reality is that it remains incurable despite significant progress in treatments. Patients who progress after both a BTK and BCL2 inhibitor fail face a poor prognosis with few treatment options other than PI3K inhibitors.
    - Unfortunately, the use of PI3K inhibitors for hematologic malignancies has recently come under scrutiny due to safety and efficacy concerns.

Conclusion

CLL Society appreciates the opportunity to contribute the perspective of those living with CLL/SLL as CMS implements the DPNP. We look forward to a continuing dialogue throughout the IRA implementation process and welcome the opportunity to discuss our comments or the experience of CLL/SLL patients generally.

Thank you for your consideration of these comments. If you have any questions, please contact Saira Sultan, CLL Society's Healthcare Advocacy & Policy Consultant at ssultan@cllsociety.org.

Sincerely,

Brian Koffman, MDCM, MSEd
Co-Founder, Chief Medical Officer, & Executive Vice President
CLL Society

EXELIXIS®

1851 Harbor Bay Parkway
Alameda, CA 94502

650.837.7000 MAIN
650.837.8205 FAX
www.exelixis.com

May 22, 2023

BY ELECTRONIC FILING (http://www.regulations.gov)

William N. Parham, III
Director, Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
Room C4-26-05
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Information Collection Request (ICR) for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847)

Dear Mr. Parham:

Exelixis is writing to submit comments on the Centers for Medicare & Medicaid Services' (CMS) ICR for the Data Elements authorized under the Medicare Drug Price Negotiation Program (Program).[1]

Exelixis is an innovative, research-based pharmaceutical company that focuses exclusively on accelerating the discovery, development, and commercialization of new medicines for difficult-to-treat cancers. We are committed to serving patients in desperate need of more effective cancer therapies. Our discovery efforts have resulted in two available products that are marketed by Exelixis: CABOMETYX® (cabozantinib) tablets and COMETRIQ® (cabozantinib) capsules. Exelixis has a long-standing commitment to research and development (R&D) reinvestment, year-over-year investing a substantial portion of revenues derived from our commercialized products back into R&D so that we may deliver the next generation of medicines that could raise the standard of care for patients with cancer. Before we had a commercialized product, we spent between 73 percent and 87 percent of operating expenses on R&D (nearly $2.3 billion). In 2022, Exelixis invested approximately 55 percent of our revenue in R&D,[2] and in the first quarter of 2023, we invested approximately 57 percent of our revenue in R&D.[3]

We incorporate by reference comments from our trade association, the Biotechnology Innovation Organization (BIO). We are commenting here on issues of particular importance to

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[1] 88 Fed. Reg. 16983 (Mar. 31, 2023); forms *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847 (Data Elements ICR).
[2] Exelixis, *Exelixis Announces Fourth Quarter and Full Year 2022 Financial Results and Provides Corporate Update* (Feb. 7, 2023), https://ir.exelixis.com/news-releases/news-release-details/exelixis-announces-fourth-quarter-and-full-year-2022-financial.
[3] Exelixis, *Exelixis Announces First Quarter 2023 Financial Results and Provides Corporate Update* (May 9, 2023), https://ir.exelixis.com/news-releases/news-release-details/exelixis-announces-first-quarter-2023-financial-results-and.

Exelixis, presenting the perspective of a midsize biotech on a mission to help cancer patients recover stronger and live longer. Exelixis' comments can be summarized as follows:

- CMS' intended definition of "R&D" is too narrow, and it should be broadened to reflect commonly accepted R&D costs. In particular, CMS should expand the ICR to permit reporting of: (1) costs arising from manufacturer investigations of indications that have not been FDA-approved; (2) costs for all failed or abandoned products; (3) costs associated with ongoing trials; and (4) indirect expenses at all phases of R&D.

- For cancer medicines, consistent with the Cancer Moonshot and CMS' protected classes policy, CMS should establish the "starting point" for the maximum fair price (MFP) initial offer at the selected drug's ceiling price—not the Part D net price or average sales price (ASP) of its therapeutic alternative(s).

- CMS should clarify that therapeutic alternatives will be identified based on their clinical characteristics and value, not cost factors. It is critically important that CMS adopt a flexible approach to defining value that prioritizes widely accepted clinical guidelines, as well as patient perspectives. Because the determination of therapeutic comparability is fundamentally a medical one, CMS should release its list of proposed therapeutic alternatives and provide stakeholders the opportunity to comment on those alternatives before CMS makes the MFP initial offer.

I. R&D Costs and Recoupment (Section C)

The IRA requires manufacturers of selected drugs to submit to CMS data regarding "[r]esearch and development costs of the manufacturer for the drug and the extent to which the manufacturer has recouped research and development costs."[4] The ICR proposes that manufacturers would report their R&D costs in the following six categories: (1) basic pre-clinical research costs, (2) post-Investigational New Drug (IND) application costs, (3) completed U.S. Food and Drug Administration (FDA)-required Phase IV clinical trials, (4) post-marketing trials, (5) abandoned and failed drug costs, and (6) all other R&D costs.[5] Primary Manufacturers would also report their "global, total lifetime net revenue for the selected drug," which CMS would use to determine whether a selected drug's R&D costs have been recouped.[6]

Exelixis believes that this proposal disregards legitimate R&D costs that are necessary and unavoidable to discover, develop and deliver the next generation of life-saving medicines for patients, while also imposing significant and unnecessary reporting burdens on manufacturers. We are concerned that CMS' narrow view of R&D will disproportionately impact oncology-focused biotechs, like Exelixis, which take on some of the greatest risks. This is not only bad policy, but it directly contradicts the clear Congressional intent to protect R&D incentives for

[4] Social Security Act (SSA) § 1194(e)(1)(A).
[5] Data Elements ICR at 5.
[6] *Id.* at 6.

smaller biotechs.[7] As we have stated in our prior comments on the Small Biotech Exemption[8] and the Program's Initial Guidance,[9] we urge CMS to carefully consider the impact of its policies on small and mid-size biotechs, like Exelixis, that drive a significant share of medical innovation. CMS should use its authority to implement the IRA in a manner that protects, not harms, companies like Exelixis. Therefore, with respect to this ICR, we urge CMS to expand the scope of R&D costs, consistent with our recommendations below.

A. CMS Should Not Limit R&D Costs to Labeled Indications (Instructions for Questions 1 to 6)

In the instructions for reporting R&D costs, the ICR states that unless otherwise specified, manufacturers should "not report any costs for indications that are not labeled indications."[10] The instructions for the following questions expressly limit reporting to FDA-approved indications: basic preclinical research (Question 1); post-IND research (Question 2); FDA-required phase IV trials (Question 3); post-marketing trials (Question 4). The instructions for the questions related to failed or abandoned products (Question 5) and all other R&D costs (Question 6) do not state whether reporting is limited to FDA-approved indications.

Exelixis strongly opposes limiting the eligibility of R&D costs to costs incurred for labeled indications because such a limitation ignores the reality that, for each successful clinical trial leading to a labeled indication, companies have likely invested in numerous clinical trials in alternative indications that proved to be unsuccessful. For most companies, the road to clinical and commercial success is long, uncertain and arduous. While laboratory models and animal testing can help scientists understand a compound's potential, the only way to truly explore a promising therapy's full benefit is clinical trial and error. Oncology-focused biotechs, like Exelixis, do not merely invest with confidence in single indications; they investigate the therapeutic possibilities of their candidate products broadly, narrowing their experiments over time. These investments begin long before any indications are ultimately approved, and after a single indication is approved, successive investments aim to broaden the utility of the product for additional patient populations.

Exelixis' experience with cabozantinib illustrates this challenge. Cabozantinib is the active ingredient in both of Exelixis' marketed products (COMETRIQ® and CABOMETYX®). It was first approved by the FDA in 2012, as COMETRIQ®, to treat a small number of patients with a rare thyroid cancer. Based on this early success and encouraging evidence from smaller,

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[7] *See* Chairman Ron Wyden, *Principles for Drug Pricing Reform* 1 (June 2021), https://www.finance.senate.gov/imo/media/doc/062221%20SFC%20Drug%20Pricing%20Principles.pdf (stating that because ""[t]he research that led to these medical advances can largely be traced back to small biotechnology companies that take on a disproportionate share of the risk of R&D," drug pricing reforms should be ""tailored to the scale of these companies, as well as other factors that affect their access to capital" (emphasis added)).

[8] Exelixis Comments to CMS on Small Biotech Exception ICR (March 27, 2023), https://www.regulations.gov/comment/CMS-2023-0008-0004.

[9] Exelixis Comments to CMS on the Program Initial Guidance (submitted April 14, 2023).

[10] Data Elements ICR at 6.

early-stage clinical trials, Exelixis launched a broad, late-stage clinical development program in a range of solid tumor indications. However, in 2014, results from the first two of these larger global pivotal trials, which focused on prostate cancer, were negative. The impact upon the company was catastrophic. We had to restrict spending immediately, including by reducing our workforce by more than 70 percent, to conserve our limited financial resources while we waited for results from two additional global pivotal trials in kidney and liver cancer. Fortunately, cabozantinib demonstrated positive results in these studies and received FDA approval in 2016 as CABOMETYX®. Today, it is a leading therapy for three different forms of cancer and a standard of care for renal cell carcinoma. Moreover, based on critical information gleaned from the earlier cabozantinib prostate cancer studies, which were negative, we are again testing cabozantinib for the treatment of prostate cancer, this time in combination with immunotherapy, and are hopeful that these studies will read out positive later this year. As currently contemplated, however, Questions 1 to 4 would not consider Exelixis' extensive research investments related to cabozantinib in prostate cancer, because prostate cancer is not a labeled indication.

The entire history of preclinical and clinical investigation of a promising cancer therapy, including experimental failures and successes, is both scientifically necessary and useful to physicians who prescribe that therapy. Exelixis therefore requests that CMS revise the instructions for Questions 1 to 6 to permit reporting of all relevant research—regardless of whether it ultimately led to a labeled or unlabeled indication. An approach that distinguishes between labeled and unlabeled indications penalizes companies for undertaking standard scientific investigation and discourages further research on an active ingredient or active moiety after the first indication has been approved. This approach will hit innovation in oncology the hardest – to the detriment of patients. The tough reality is that although our research informs us of which indications to pursue, not all trials will necessarily succeed. "Failed" trials, however, are an important part of the development effort and often yield important findings that benefit patients (e.g., treatment benefits in sub-populations). Therefore, we strongly urge CMS to recognize equally the value of all R&D investments, not only those that were ultimately successful. At a minimum, CMS should clarify that Questions 5 and 6 permit reporting of R&D costs related to unlabeled indications, which we believe is consistent with CMS' current intent for these questions.

B. CMS Should Consider R&D Costs for All of a Manufacturer's Failed or Abandoned Products (Question 5)

Question 5 of the ICR proposes that the Primary Manufacturer "allocate a portion of the direct costs spent on basic research, preclinical research, and clinical research for failed or abandoned products related to the selected drug."[11] The ICR instructs manufacturers to "only include costs that can be directly attributed to failed or abandoned product(s) with the same

[11] *Id.* at 11 (emphasis added).

active moiety / active ingredient or mechanism of action *or* drugs in the same therapeutic class as the selected drug that did not achieve FDA approval."[12]

Exelixis believes that it is not appropriate to limit "failed or abandoned product costs" to costs related to the selected drug. We are concerned that the ICR's intended approach would completely disregard our significant investments on a broad platform of anticancer targets to ultimately arrive at the one that is improving patients' lives worldwide. Given the overwhelming challenges and inherent risks at every stage of the discovery, development, regulatory, and commercialization process, we request that CMS consider the full scope of a manufacturer's failed or abandoned product costs.

C. CMS Should Consider Costs Associated with Ongoing Clinical Trials (Instructions for Questions 1 to 7)

The ICR's instructions for reporting R&D would exclude certain costs, including "costs related to *ongoing* basic preclinical research, clinical trials, and pending approvals."[13] Exelixis opposes this limitation and strongly encourages CMS to consider a manufacturer's ongoing clinical trial expenses during the MFP determination process. This is particularly important for oncology medicines, where manufacturers often make substantial investments in existing products, including new indications for different patient populations and improvements to the formulation. This also would create an important incentive for manufacturers of selected drugs to continue their R&D investments.

D. CMS Should Consider Direct and Indirect Research Expenses Comprehensive of All R&D Phases (Questions 1 to 6)

Question 1 directs manufacturers to report "*total R&D costs* incurred by the Primary Manufacturer for all FDA-approved indications for the selected drug related to basic preclinical expenses."[14] The ICR explains that total R&D costs would include "[d]irect research expenses . . . that can be specifically attributed to the discovery and preclinical development of the selected drug"[15] and "[i]ndirect research expenses and relevant general and administrative expenses."[16] However, after the preclinical research phase, the ICR directs manufacturers to report their "direct costs" in response to the following questions: post-IND application costs (Question 2), completed FDA-required phase IV trials (Question 3), post-marketing trials (Question 4), and

[12] *Id.* at 12 (italics in original).
[13] *Id.* at 5 (italics in original).
[14] *Id.* at 7 (italics added).
[15] "Direct research expenses are costs that can be specifically attributed to the discovery and preclinical development of the selected drug. Direct research expenses could include personnel (compensation for investigators and staff) researching the selected drug, materials for conducting basic preclinical research, and the costs of in vivo and in vitro studies on the selected drug before an IND application went into effect." *Id.*
[16] "Indirect research expenses and relevant general and administrative expenses are operating costs for basic pre-clinical research beyond the basic pre-clinical research costs for the selected drug, including administrative personnel and overhead costs (expenses for clinical facilities and equipment) that are shared across multiple potential drugs or biologics." *Id.*

abandoned and failed drug costs (Question 5).[17] It is unclear whether manufacturers are permitted to report indirect expenses in response to Question 6, which is a catchall for "costs it attributes to [R&D] that were not accounted for in Questions 1 through 5."[18]

We strongly encourage CMS to clarify that manufacturers should report, and CMS will consider, total R&D costs (i.e., direct and indirect expenses) across all stages of research. In order for Exelixis to successfully run an oncology development program, we require infrastructure in the form of facilities, equipment, and support functions. We urge CMS to consider the entirety of R&D expenditures, both direct and indirect, which are a necessary part of research at all phases. Therefore, CMS should permit manufacturers to report their indirect expenses in response to Questions 2 through 5; or at a minimum, CMS should clarify that manufacturers may report indirect expenses in response to Question 6, which we believe is consistent with CMS' intent for this question.

II. Evidence About Alternative Treatments (Section H)

A. The MFP Starting Point for Cancer Drugs Should Be Based on its Ceiling, Not the Cost of Therapeutic Alternative(s)

The Initial Guidance intends to use the Part D net price or the Part B ASP (as applicable) of a selected drug's "therapeutic alternative(s)" as the "starting point" for the MFP initial offer.[19] Exelixis disagrees with this approach, which in many cases will undervalue selected drugs. Exelixis also is concerned that tying selected drugs to the price of therapeutic alternatives will erode incentives to develop next-generation medicines that could markedly improve treatment, or even save lives.

At a minimum, Exelixis requests that CMS adopt a different approach for calculating the initial offer for selected drugs with cancer indications. For such drugs, Exelixis requests that CMS set the "starting point" for the MFP at the ceiling price of the selected drug, not the Part D net price or ASP of its therapeutic alternative(s). In other contexts, CMS has granted cancer medicines special protections. For example, the six protected classes policy requires Part D plans to cover "all or substantially all" of medicines in certain classes, including antineoplastics.[20] By requiring access to "all or substantially all" of medicines within these classes, CMS recognizes that protected class drugs are unique and are not interchangeable. Our proposed approach to calculating the MFP for cancer drugs would also foster incentives for innovation of cancer drugs,

[17] (emphasis in original).
[18] *Id.* at 12.
[19] CMS, Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (Initial Guidance) § 60.3.1 (Mar. 15, 2023), https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.
[20] *See* CMS, Medicare Prescription Drug Benefit Manual Chapter 6—Part D Drugs and Formulary Requirements, § 30.2.5.

consistent with the Administration's Cancer Moonshot and its mission to "accelerate the rate of progress against cancer."[21]

B. CMS Should Identify Therapeutic Values Based on Clinical Value, Not Cost (Questions 40 to 43).

The Initial Guidance provides that to identify potential therapeutic alternatives, CMS intends to:

(1) Use data submitted by the Primary Manufacturer and the public, FDA-approved indications, indications included in CMS approved Part D compendia, widely accepted clinical guidelines, and peer-reviewed studies.

(2) Consider clinical evidence available through literature searches when a therapeutic alternative has not yet been incorporated into nationally recognized, evidence-based guidelines.

(3) Begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes.[22]

Under this ICR, the Primary Manufacturer and members of the public *may* provide CMS with certain information about therapeutic alternatives, including: FDA-approved prescribing information (Question 40); therapeutic impact (Question 41); comparative effectiveness with respect to specific populations (Question 42); and the extent to which the medicine meets an unmet medical need (Question 43).

In determining a medicine's value, Exelixis strongly encourages CMS to adopt a flexible approach and to avoid one-size-fits-all criteria that treat all medicines or indications in the same manner. For example, the measures of value for a medicine that treats a life-threatening cancer condition may differ significantly from the measures of value for an antidepressant. Moreover, in certain cases, the measure of value of a selected drug could differ between its indications. For example, a measure of value for a colorectal cancer indication may be a complete cure, while the measure of value for the same drug in metastatic liver cancer could be symptom relief or increased quality of life.

Exelixis also supports CMS' intention to consider the clinical value of selected drugs based on widely accepted clinical guidelines. For cancer drugs, Exelixis recommends that CMS consult the National Comprehensive Cancer Network's (NCCN) Guidelines, which are rigorously developed guidelines that apply to nearly all cancers affecting patients in the United

[21] White House, *Cancer Moonshot*, https://www.whitehouse.gov/cancermoonshot/.
[22] Initial Guidance § 60.3 (line breaks added).

States.[23] Specifically, Exelixis recommends that CMS consider medicines that are recommended under Category 1 [Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate] or Category 2A [Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate].

Finally, CMS should establish a transparent process for identifying therapeutic alternatives with multiple opportunities for stakeholder engagement. At a minimum, Exelixis recommends that CMS publish a list of therapeutic alternatives that the Agency is considering concurrently or as soon as possible after the selected drugs list is published on September 1, 2023. It is important that stakeholders have a chance to consider CMS' proposed list of therapeutic alternatives when developing their responses to this ICR. Moreover, because therapeutic comparability is fundamentally a medical determination, CMS should conduct targeted outreach to solicit input on the potential therapeutic alternatives from the clinical community. CMS also should solicit feedback from a diverse group of patients to learn about their personal experiences and perspectives on the potential therapeutic alternatives. In addition to this ICR, Exelixis encourages CMS to consider roundtables, public meetings, and other ways to solicit feedback from relevant stakeholders.

* * *

The Administration's Cancer Moonshot calls on the "[p]rivate sector to step up -- to develop and test new treatments."[24] We are now returning the same call to you. We strongly encourage CMS to implement the IRA in a manner that fosters incentives for the next generation of cancer medicines for patients across America.

We hope that CMS will take these comments into consideration when developing the revised Data Elements ICR. We would be happy to answer any questions that CMS may have regarding the topics we address herein.

Sincerely,

Michael M. Morrissey, Ph.D.
President and Chief Executive Officer
Exelixis, Inc.

[23] NCCN, *Development and Update of Guidelines*, https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines.
[24] White House, *Cancer Moonshot*, https://www.whitehouse.gov/cancermoonshot/.

Genentech
A Member of the Roche Group

600 Massachusetts Ave. NW, Suite 300
Washington, DC 20001
Phone: (202) 296-7272
Fax: (202) 296-7290

May 22, 2023

William N. Parham, III, Director
Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
Centers for Medicare & Medicaid Services
7500 Security Boulevard Baltimore, Maryland 21244

Sent via electronic mail

Re: Comments on *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)*

Dear Mr. Parhnam:

Genentech appreciates the opportunity to submit comments on the *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)* (the "ICR"). We agree with CMS' stated goal of the ICR to ensure that the collection of information specific to the negotiation factors under the Inflation Reduction Act ("IRA") is clear, reduces burden and duplicative reporting, and collects only relevant information needed for the proper implementation of the IRA's Medicare Drug Price Negotiation Program (the "Program"). Below we provide comment on ways CMS could best achieve these goals.

Genentech is a leading biotechnology company dedicated to pursuing groundbreaking science to discover and develop medicines for people with serious and life-threatening illnesses. We are committed to improving patients' lives through new innovations. To this end, in 2022 we, under the Roche umbrella, invested over $15 billion globally in research and development – more than any other health care company in the world. In the past ten years, we have delivered to patients 20 new medicines that treat devastating diseases like cancer, multiple sclerosis, and hemophilia. In addition to our over 40 approved medicines, we have 70 potential new medicines in clinical or preclinical development and have been granted 39 FDA Breakthrough Therapy Designations for medicines with the potential to provide substantial improvement over currently available treatments. It is this commitment to innovation and treatment advances we feel should be incentivized through the IRA process. Because collecting information from manufacturers is a critical step in the IRA, proper implementation of this ICR is similarly critical, including reducing the burden of reporting and ensuring the confidentiality of sensitive information.

Consistent with the requirements of the Paperwork Reduction Act (PRA), our comments focus on: 1) the necessity and utility of the proposed information collection for the proper performance of CMS' functions as it relates to the Program; 2) the accuracy of the estimated burden; and 3) ways to enhance the quality, utility, and clarity of the information to be collected. Particularly given the extremely limited time manufacturers will have to respond to the ICR after their drugs are selected for negotiation, it is of paramount importance that CMS collect only those data elements essential to CMS' implementation of the Program to which the government does not already have access. It is also critical that CMS ensure the information collected is of high quality, utility, and clarity given the Program's potential to significantly impact patient access and the incentives for future innovation.

As outlined in Section I of our comment letter, below, in general we recommend that CMS revise the ICR to:

- Solicit information directly from Secondary Manufacturers to avoid placing all data collection and reporting responsibility on Primary Manufacturers;
- Reduce manufacturer burden by embracing industry accounting standards and relying on information already reported by manufacturers where possible;
- Be more flexible regarding allowable data submission formats by allowing rolling submissions, increasing word limits, and allowing additional data formats for therapeutic alternative data; and
- Provide transparency for manufacturers of selected drugs regarding therapeutic alternative data considered by CMS.

Consistent with these general recommendations, we also provide comments specific to each of the ICR's questions in Section II of our comment letter.

I. General Comments and Recommendations

A. Collect information directly from Secondary Manufacturers to ensure CMS is able to collect the necessary information for Program implementation while reducing burden on Primary Manufacturers.

As described in the initial Program guidance[1] and this ICR, CMS proposes to establish a paradigm whereby Primary Manufacturers are required to report aggregated data, including data regarding each of the section 1194(e)(1) negotiation factors, for the selected drug for both the Primary Manufacturer—which CMS defines as the manufacturer that owns the New Drug Application or Biologics Licensing Application for the selected drug—and any Secondary Manufacturer(s). As previously commented, Genentech is concerned that this approach imposes an undue burden on the Primary Manufacturer by requiring the Primary Manufacturer to collect sensitive and proprietary information from distinct legal entities and report it to CMS.

[1] Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (March 15, 2023), https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.

Additionally, this paradigm fails to recognize that co-development, co-commercialization, certain organizational structures, and other partnership agreements must often maintain strict firewalls and often involve legal requirements that prevent the sharing of certain data between entities, making it difficult if not impossible for the Primary Manufacturer to report all of the necessary data. This paradigm thus exposes Primary Manufacturers to unnecessary legal risk. It also imposes liability on the Primary Manufacturers for the accuracy and completeness of information and data that is maintained by an independent legal entity, needlessly imposing on Primary Manufacturers the additional burden of submitting data requests to Secondary Manufacturers, following up as necessary, reconciling differences in data management and accounting methodologies, and finally blending various sales data, all without clear instruction or support from CMS. None of this is necessary for the proper implementation of the Program.

Instead, to reduce burden on Primary Manufacturers and increase the utility, clarity, and quality of the data collected, CMS should establish agreements with Secondary Manufacturers of each selected drug, consistent with the requirements of section 1193 of the Social Security Act (the "Act"), and solicit information regarding the section 1194(e)(1) negotiation factors directly from Secondary Manufacturers via this ICR. This would ensure a complete data picture and transparency between CMS and all manufacturers of selected drugs, and would eliminate the need for manufacturers to exchange sensitive data, such as pricing information.

B. Leverage existing industry standards and data already available to the agency to reduce burden on manufacturers.

CMS estimates that it will take 500 total hours per manufacturer to collect and calculate the information required under the ICR. Unfortunately, this is a gross underestimation due to the non-standard data types and overly segmented nature of the data CMS is requesting. Although CMS instructs manufacturers to calculate the requested data consistent with manufacturers' own accounting policies and industry standards, this ICR ignores industry standards in its instructions. Adding to the burden is the large amount of duplicative reporting outlined in this ICR; that is, CMS is requesting multiple data points that are either already reported to the government or available publicly. We recommend that CMS instead leverage existing industry standards and data already available to the agency to reduce burden on manufacturers. Specific suggestions to address these recommendations are included in Section II below.

C. Reduce burden and improve information collected by allowing rolling submission of requested data, increasing word limits, and permitting the upload of related tables and figures.

We continue to urge CMS to establish a data submission process that allows manufacturers to supplement the information reported by the submission deadline (which is only 30 days after drug selection) on a rolling basis. CMS already instructs manufacturers to notify the agency if submitted information has changed, which indicates that CMS is capable of receiving additional information after the submission deadline and prepared to do so. Allowing rolling submissions would improve the quality, utility, and clarity of the information collected by allowing manufacturers ample time to submit responsive information and supplementing that information as needed.

We also note that limiting the data submission to word text is too limiting and will not allow stakeholders to highlight the most relevant information. To enhance the quality and utility of the data, CMS should include an upload option for information like tables and figures. Additionally, limiting citations to "published" materials is limiting and would exclude relevant and informative data sources. Therefore, we recommend that CMS define "published material" to include information conveyed at relevant medical congress proceedings (e.g., posters, summaries, or documents of presented materials). CMS should also allow for manufacturers to submit relevant data on file, which may not be in the public domain and to mark such data as proprietary and not subject to release.

We agree with CMS that providing free text boxes to provide additional detail or discuss assumptions and methodologies is important to enhance the utility, quality, and clarity of the information. However, CMS has arbitrarily chosen to institute varying word limits for each free text box. Some responses will naturally require fewer words than others, but placing arbitrary limits on the length of each response can lower the quality of the submission by potentially requiring manufacturers to omit relevant information just to comply with the imposed word limit. To allow manufacturers maximum flexibility, we recommend CMS choose a 5000-word limit to accommodate more lengthy responses, especially for data related to therapeutic alternatives. We also recommend that CMS permit manufacturers to append relevant information to their submissions, an option that may also relieve the some of the issues that arise due to word limitations.

D. Provide transparency for manufacturers of selected drugs regarding therapeutic alternative data considered by CMS.

Transparency into key decision points made by CMS as well as access to non-proprietary data used to evaluate therapeutic alternatives is critical to the successful operation of the Program. CMS should also ensure that manufacturers are provided access to the evidence submitted on therapeutic alternatives. To facilitate this, CMS could require any stakeholder submitting information under Section H (Evidence About Alternative Treatments) to indicate whether the evidence is proprietary or non-proprietary. Any non-proprietary data should be shared with the manufacturer(s) of the selected drug.

II. Section-Specific Comments

A. Section A: Selected Drug Information

Section A of the ICR proposes to require the Primary Manufacturer to list all NDC-11s of the selected drug, including any NDC-11s marketed by any Secondary Manufacturer(s). We reiterate our earlier comment that **CMS collect information directly from Secondary Manufacturers of a selected drug** regarding the negotiation factors specified in section 1194(e)(1) to improve the quality, utility, and clarity of the information collected and reduce the burden on Primary Manufacturers of responding to this ICR.

B. Section B. Non-FAMP Data Collection

Section B of the ICR proposes to require the submission of certain information related to non-FAMP. This metric is duplicative as manufacturers already report non-FAMP data to the government. However,

if CMS will require manufacturers to report non-FAMP to HHS, **we recommend that manufacturers be permitted to utilize the non-FAMP data reported elsewhere to the government to reduce burden**.

C. Section C: Research & Development Costs and Recoupment

Section C of the ICR contains seven two-part questions: (1) dollar amounts for R&D and recoupment costs; and (2) explanations of how those costs were calculated, where applicable. **As stated in our comment letter to the initial Program guidance, we believe that CMS should consider data on the manufacturer specific factors only when a product provides fewer benefits compared to therapeutic alternatives.** However, it is still important for CMS to provide clarity, where possible, on the specific reporting requirements for these factors to ensure the data collected is useful and of the highest quality. CMS should also take steps to ensure that the reporting of this information is not imposing unnecessary burden on manufacturers. To these ends, **we recommend that CMS streamline R&D cost reporting requirements, align R&D cost recoupment data collection with the statute, and broaden the definition of R&D costs to capture the full costs of drug development.**

i. Streamline R&D cost reporting requirements.

When requesting information on R&D costs, CMS instructs Primary Manufacturers to parse out their R&D costs in six separate sub-categories without any explanation or justification. Separating out R&D costs in the manner CMS has proposed is neither necessary nor required by statute, which merely directs CMS to consider "research and development costs of the manufacturer for the drug and the extent to which the manufacturer has recouped research and development costs." These instructions also don't align with industry standard accounting practices for R&D costs and would not accurately reflect the dynamic and risk-based approach to making drug discovery investments generally employed by industry. Thus, CMS has arbitrarily increased manufacturer burden with useless calculations and reporting that do not enhance the quality, utility, or clarity of the information. Indeed, breaking down R&D costs as proposed by CMS could actually distort the drug development picture, preventing CMS from drawing useful conclusions regarding overall R&D costs as required by statute.

To reduce this burden and improve the quality and utility of the information collected, **CMS should instead focus on the holistic R&D costs for the drug—for both the Primary Manufacturer and any Secondary Manufacturers—in two broad categories: (1) total aggregated costs of R&D before initial FDA approval, and (2) total aggregated costs of R&D after FDA approval.**

ii. Broaden definition of R&D costs to capture the full cost of drug development.

CMS instructs manufacturers to exclude certain global costs of R&D, like costs related to indications approved only ex-U.S. Yet CMS requests global, total lifetime net revenue data which will inevitably include sales for indications not approved in the U.S. This inconsistency is arbitrary, lowers the quality of data being requested, and will hinder the agency's proper administration of the Program. **To ensure CMS has the full scope of R&D costs, and to the extent CMS requires manufacturers to report global, total lifetime net revenue, these calculations should include *all* global costs.**

CMS' proposed collection of R&D cost data also does not reflect how manufacturers approach drug development. In particular, CMS proposes to consider only those R&D costs incurred by the Primary Manufacturer. This approach does not take a holistic view of the role of each manufacturer in developing a selected drug by limiting the consideration of R&D cost data to that only of the Primary Manufacturer. Indeed, Secondary Manufacturers can incur certain R&D costs that will later be used to support the Primary Manufacturer's NDA/BLA filing. For these, **CMS should collect and consider R&D costs from Secondary Manufacturers to greatly enhance the utility and quality of the requested data.**

We also note that CMS excludes important sources of R&D costs that influence investment decisions which lowers the quality and utility of the data submitted. Due to the inherent risk in drug development manufacturers will purposefully diversify risk across the entire portfolio and then cross-subsidize over different therapeutic areas or mechanisms of action. The drug development successes enable further research and allow manufacturers to take risks that may never pan out. It is important to remember that the areas of most unmet need are often some of the riskiest areas to develop medicines (e.g., Alzheimer's disease). Therefore, **we feel strongly that R&D costs should include the cost of failures from research areas that never had a drug come to market.**

Drug development takes many paths and may include partnerships or acquisitions that bring needed knowledge and funding to support continued development, bring new capabilities or efficiencies, enhance efforts to scale up production, or any number of added benefits. Ultimately this activity furthers advancements in science that can bring innovative drugs that address unmet needs to market. For these reasons, **manufacturers should be permitted to include acquisition costs (of marketed and failed drug candidates), partnering agreements, or any other in-licensing development agreement in R&D costs.**

iii. Align R&D cost recoupment data collection with statute.

CMS is also collecting unnecessary information regarding recouped R&D expenditures. Specifically, CMS proposes to use the Primary Manufacturer's global, total lifetime net revenue for the selected drug to determine the extent to which the Primary Manufacturer has recouped R&D costs for the selected drug. **This can be most simply accomplished with the least burden by replacing Question 7 with a single attestation (YES/NO) on whether a manufacturer has recouped their R&D costs.** We note that this approach is also consistent with the statute, which does not specifically reference information regarding global revenues, and instead merely refers to "[r]esearch and development costs of the manufacturer for the drug *and the extent to which the manufacturer has recouped research and development costs*."[2]

D. Section D: Current Unit Costs of Production and Distribution

Section D contains two questions on current unit costs of production and distribution for the selected drug, including a table to report the average unit costs of production and distribution for each NCD-9, and a free response field to report the methodology used. We recognize the statute includes as a factor "[c]urrent unit costs of production and distribution of the drug"; however, CMS' instructions for

[2] SSA § 1194(e)(1)(A) (emphasis added).

calculating unit costs of production and burden do not align to industry standards and therefore impose needless burden by requiring manufacturers to calculate data in a manner that does not provide additional utility or quality. Production costs are often not calculated at the NDC level from an accounting perspective. In addition, detailed information on production costs may simply not be available if a partner or other entity conducted some or all of the manufacturing. Instead, **CMS should provide discretion to manufacturers to calculate production and distribution costs in a manner that aligns with industry standards,** rather than specifying a detailed methodology that may not mirror how these costs are recorded and tracked.

E. Section E: Prior Federal Financial Support

Section E of the ICR focuses on capturing prior federal financial support for novel therapeutic discovery and development with respect to the selected drug. We reiterate our earlier comment that CMS should collect data directly from Secondary Manufacturers of a selected drug to reduce burden on the Primary Manufacturer and to improve the quality, utility, and clarity of the data collected. We also note that CMS' description of what constitutes federal financial support is confusing and internally inconsistent. As a threshold matter, for consistency with the statute **we recommend that CMS consider only federal financial support specific to novel therapeutic discovery and development with respect to the selected drug, and not contracts or tax credits**. We also **recommend that CMS request this information in the aggregate and only for approved indications of the selected drug.** To assist in reporting, we suggest CMS provide specific examples for each of the data points requested to ensure the information reported aligns with the information CMS needs to implement the Program.

i. Consider only federal financial support, and not contracts or tax credits.

The statutory negotiation factor refers specifically to "[p]rior Federal financial support for novel therapeutic discovery and development with respect to the drug." Consistent with this standard, CMS claims to be limiting the definition to federal financial support to funds provided by the federal government that "support discovery, research, and/or development related to the selected drug." Yet, Question 12, appears to include commercial contracts with the government given that the instructions explicitly refer to "each licensing agreement, pricing agreement, purchasing agreement, and other agreement in place between your company and the federal government agency." Question 12 also directs manufacturers to include "information on pricing, the nature and amount of goods/services agreed upon, timelines to delivering goods/services, conditions on the agreement (exclusivity, sole supplier, etc.)," and lists as an example "an agreement between the Primary Manufacturer and Federal Government where the Primary Manufacturer agrees to produce a certain quantity of a drug…"

We note that the inclusion of funds exchanged pursuant to a procurement or other contract is inconsistent with the concept of federal financial support. Indeed, in describing the circumstances in which a federal agency may use grants, cooperative agreements, and contracts, the Federal Grant and Cooperative Agreement Act of 1977 uses the term "support" only in defining grants and cooperative agreements, both of which are used to support a public purpose.[3] A government contract, on the other hand, is used to

[3] 41 U.S.C. §§ 503-505.

acquire services or property *for the direct benefit of the federal government*.[4] **We therefore recommend that CMS strike Question 12 from the ICR and clarify that "discovery, research, and/or development" does not include commercial contracts with the government.**

As outlined in Question 11, CMS also intends for tax credits to be included in calculations of prior federal financial support. As stated in our comments submitted in response to the initial Program guidance, because CMS intends to apply a downward adjustment to the starting point for prior federal financial support received, the inclusion of tax credits for this purpose is inconsistent with the intended purpose of these credits: incentivizing behavior to advance an issue of importance to the government, in this case biopharmaceutical innovation. Collecting this information is thus not necessary, will not add utility, and may actually harm CMS' implementation of the Program.

ii. For consistency with the statute, request one single number for federal financial support.

In Section E, CMS proposes to require manufacturers to disaggregate data for Prior Federal Financial Support. Here, too, CMS is going beyond the statute, which refers only to prior federal financial support as one line item. Sub-dividing the data in the way CMS proposes does not enhance the utility of the data and only serves to increase burden on manufacturers.

F. Section F: Patents, Exclusivities, and Approvals

Section F of the proposed ICR focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act.

i. CMS should not apply downwards adjustments to the initial price offering as a result of pending and approved patents, exclusivities, and FDA applications.

As a threshold matter, we reiterate our concern with CMS' proposal, as outlined in the initial Program guidance, to apply downward pressure on the initial price offering as a result of such pending and approved patents and FDA applications. This is inappropriate and counter to CMS' goals of implementing policies that protect and promote innovation. As discussed in our comments submitted in response to the initial Program guidance, patents and exclusivities award innovation by providing a time-limited opportunity to market a product without certain types of competition. Manufacturers continue to innovate through continued R&D on approved drugs to show efficacy in additional indications, improve delivery, or improve efficacy. All of these activities, to the extent they result in new intellectual property, may result in new patents or exclusivities. Placing downward pressure on the initial price offering, as CMS suggests would occur, fails to recognize that these patents were awarded to recognize significant innovation in technologies and practices that advance treatment, and will be a strong disincentive to continue to innovate after initial approval because the full value of innovation would not be realized. Collecting such information would in fact harm the proper performance of the Program.

[4] *Id.* at § 503.

We also note that the use of pending applications to inform an initial price offering as part of the Program is particularly inappropriate. Not only is this information highly confidential, but pending patent and FDA applications are not guaranteed to be approved or finalized as CMS appears to be assuming. CMS cannot draw non-arbitrary conclusions on future patents or exclusivities from pending applications. **As such, pending patent and FDA applications should not be used to inform the initial price offering.**

ii. Amend the patent-related questions in the ICR to improve data quality and clarity.

In defining relevant patents in Section F of the ICR, CMS refers to "all patent applications, pending and approved, for which a claim of patent infringement *could reasonably be*, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug in any form."[5] However, manufacturers are unable to know, ex ante, which patents a drug might infringe.

CMS also refers to "patents linked to the drug where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product)." We note that the term "patents linked to the selected drug…" is confusing because the patents CMS intends for manufacturers to report are not clear and may lead to incorrect data collection and reporting. **We suggest that CMS provide additional clarity with examples on the agency's intent behind this instruction.**

G. Section G: Market Data, Revenue, and Sales Volume Data

Questions 17 through 38 of the proposed ICR are intended to collect market data and revenue and sales volume data. We reiterate our earlier comment that CMS should collect data directly from Secondary Manufacturers of a selected drug to reduce burden on the Primary Manufacturer and to improve the quality, utility, and clarity of the data collected. We also note that these questions impose an incredible burden on manufacturers by requiring the calculation and reporting of over 100 new data points that are not clearly necessary for CMS to implement the Program, may already be within the government's control, and in some cases exceed the scope of the statute. We therefore **urge CMS to reduce the scope of the market data collected to instead rely on data already reported by manufacturers to the federal government, align data collection questions with industry standards, and eliminate questions not clearly related to the scope of the Program as outlined in statute. We also urge CMS to provide flexibility to manufacturers when calculating the remaining data collection elements.**

i. Reduce the scope of market data collected and rely instead on data already reported by manufacturers to the federal government.

In Questions 17 through 38 of the proposed ICR, CMS has proposed to define "market data and revenue and sales volume data" in Section G (Market Data, Revenue, and Sales Volume Data) in an incredibly detailed and segmented way, much of which overlaps with data manufacturers already report to the government.

[5] ICR at page 20 (emphasis added).

First, CMS is requesting manufacturers report on new data types and provide multi-year figures broken out by quarter. Across all data types, this amounts to over 100 new data points that CMS is requesting (5 years X 4 quarters X 6 price types= 120 data outputs), which is especially burdensome for the new metrics that would need to be calculated by manufacturers for the sole purpose of responding to this ICR.

Second, CMS is proposing to collect data regarding Non-FAMP, Best Price, Federal Supply Schedule Price, and Big Four Price, all of which are currently reported to the federal government. These detailed specific data requests do not provide valuable additional information to meaningfully enhance the utility, quality, or clarity of information from what is already reported through BP, AMP, and ASP.

CMS should significantly reduce the reporting burden on manufacturers by streamlining the reporting obligations and relying on data already reported to the government wherever possible. We recognize that the statute indicates that manufacturers will report "information that the Secretary requires to carry out the negotiation,"[6] and that data on the section 1194(e)(1) factors is "submitted by the manufacturer."[7] However, requiring manufacturers to resubmit these data is not necessary—as the information is already reported to the government and in many cases directly to CMS—and serves only to add time and effort that must be spent responding to the ICR.

ii. Align data collections with industry standards.

Question 19 (Wholesale Acquisition Cost Unit Price) requires manufacturers to deviate from industry standards by calculating WAC at the NDC-9 level. CMS provides no instruction on how manufacturers should average WAC data (generally reported at the NDC-11 level) to get to an NDC-9-specific WAC. However, even with more instruction the required methodology may lead to inconsistencies across data points. Therefore, **CMS should allow manufacturers to submit WAC data that aligns with industry standard reporting.**

iii. Eliminate data collection questions that are outside the scope of statute.

Question 21 - 24 (340B Ceiling Price and 340B Prime Vendor Price) request information that has no bearing on the Program. These data do not provide useful information and should not be used to inform the initial price offering for the selected drug. Additionally, collection of these price types goes beyond the IRA statute, and thus would be inconsistent with the goals of the PRA to reduce burden and collect useful information.

Particularly concerning is that CMS is requesting average commercial price information net of patient assistance, suggesting that CMS intends to treat patient assistance programs as some form of price concession. Collection of price types that are net of patient assistance programs is inconsistent with statute and recent court rulings affirming that patient assistance is meant for patients and is not part of the sales price to purchasers.[8] Patient assistance programs are not even considered or discussed when

[6] *See* SSA § 1193(a)(4).
[7] *See* SSA § 1194(e)(1).
[8] *Pharmaceutical Research and Manufacturers of America v. Becerra*, No. 1:21-cv-01395 (D.D.C. May 17, 2022) (holding that a patient assistance program is not a price offered by manufacturers to payors).

developing contracting strategies with commercial entities, further illustrating that patient assistance is not and should not be viewed as a price concession. Therefore, this information is not appropriate to consider when setting the initial price point. Collecting and considering this data is unnecessary, has no utility, will lower the quality of the data, and hinder the proper implementation of the Program. **We recommend that CMS exclude this data collection from the ICR.**

iv. Provide flexibilities regarding the calculation methodology of new price types.

Generally, CMS appears to intentionally leave calculation methodologies for the new price types open to manufacturer interpretation. However, this exposes manufacturers to potential liability if CMS ultimately disagrees with calculation methodologies. This is especially troublesome because these detailed calculations go beyond statute, are not necessary to the proper implementation of the Program, and can be easily substituted with meaningful information from data that is already reported (BP, AMP, ASP). **Therefore, to the extent that CMS requests new price types, we urge CMS to provide manufacturers maximum flexibility in their calculation methodology.**

We also **urge CMS to expressly permit manufacturers the flexibility to make certain assumptions.** Question 31 (U.S. Commercial Average Net Unit Price) asks manufacturers to exclude Medicare price and volume information at point of sale, yet for Medicare Advantage data, Medicare reimbursement occurs after the fact. In order to complete this calculation certain assumptions need to be made. This situation is acknowledged by CMS for calculations of AMP. Similar allowances should be made here.

H. Section H: Evidence About Alternative Treatments

Section H of the proposed ICR solicits information about alternative treatments. Unlike the manufacturer-specific factors, which are "submitted by the manufacturer," the statute does not specify the origin of the alternative treatment data under the Program. Given the importance of the alternative treatment factors to the negotiation process, **Genentech strongly supports the collection of these data from multiple stakeholders including patients, their caregivers, providers, and manufacturers**. Indeed, as previously commented Genentech **feels strongly that CMS should establish an MFP at the ceiling price for products that, over the course of the product's lifecycle, have provided therapeutic advancements or treated previously unmet medical needs.** These data are critical to make that determination. In order to ensure the collection of the highest quality data that will have the most utility, CMS should provide additional clarity and detail on specific key definitions. **We also recommend that CMS convene stakeholder panels, in addition to collecting data through the ICR, to help inform key agency decision points during the negotiation process.**

i. Transparent process for selection of therapeutic alternatives and relevant metrics.

CMS does not indicate the type of information regarding the section 1194(e)(2) factors that the agency finds most useful, nor how CMS intends to select therapeutic alternatives of interest. This creates uncertainty that will add to the burden on manufacturers of responding to the ICR, and may result in the provision of highly inconsistent data across respondents. To prevent this, **CMS should publicly identify the therapeutic alternative(s) it intends to focus on and solicit input from manufacturers and others**

on this key decision point. CMS should also clearly list the comparative effectiveness outcomes of most interest to the agency for each selected drug, and solicit input on both those measures and the measures CMS should consider in evaluating the drug and its therapeutic alternatives. We further **recommend that CMS convene stakeholder panels to assist the agency in identifying the initial list of therapeutic alternatives and comparative effectiveness outcomes.**

Genentech believes that the comparative effectiveness outcomes of interest should include factors that impact patients and the health system, including disease outcomes, treatment adherence, patient preference, patient-reported outcomes, changes in healthcare resource utilization, cost offsets, and total cost of care. Without clear guidance on the measures under consideration and on how CMS plans to weight or prioritize different types of evidence, it is not possible for respondents to effectively prioritize and synthesize the evidence most useful to assist CMS with its determinations.

Recommended metrics and preferred evidence types should also be provided for health outcomes, surrogate endpoints, intermediate outcomes, and patient experience measures. Specifically, **CMS should provide a preferred hierarchy of evidence to best guide data collection and to help respondents to identify available data sources of most interest to CMS.** This hierarchy of evidence should identify CMS' preferences among evidence types for comparative effectiveness data (e.g., clinical trials, observational data) as well as CMS preferences among types of observational data that characterize patient and health system outcomes (e.g., Medicare claims, commercial claims, patient surveys).

For Question 42 (Comparative Effectiveness on Specific Populations), it is also unclear how CMS will combine, or weight, comparative effectiveness data across a selected drug's indications and therapeutic alternatives, which may lead to collection of irrelevant data and may unnecessarily increase the data burden for respondents. We recommend that **CMS include instructions on prioritization of the desired comparative effectiveness outcomes, including information on how CMS would like data presented/synthesized when robust comparative effectiveness research is not possible or has important data gaps for rare diseases or situations with heterogeneous populations.**

ii. Definitions for key terms should be clear.

CMS fails to provide definitions for key terms in Section H. **We recommend that CMS adopt the following definitions and considerations to enhance the clarity, quality, and utility of the information submitted in response to Section H.**

Therapeutic advance: CMS should provide an exact definition of therapeutic advance that aligns with other organizations in the US government, including existing CMS definitions for New Technology Add-on Payment (NTAP) and the FDA's definition of unmet medical need, to optimize synthesis of relevant data but also to signal the types of health improvements that CMS will value for future drug development. We recommend that a drug be deemed a therapeutic advance if one or more of its indications represents:

- Significant improvement in clinical outcomes, as assessed by patients with lived experience with the disease. For purposes of this analysis, CMS should establish a standard similar to the

substantial clinical improvement criterion used by CMS to determine eligibility for the New Technology Add-on Payment (NTAP); OR

- Improvements on a validated clinical outcome assessment,[9] for the disease state; OR
- Measurable positive impact in vulnerable populations (e.g., socially vulnerable or disadvantaged, low socioeconomic status, disabled) that could help improve health disparities.

Comparative effectiveness: CMS should list the exact type of comparative effectiveness data requested. This should include information on: (1) acceptable data types across the indications for selected drugs (i.e., clinical trial, real world evidence, Medicare claims), as comparisons will need to be made across indications and therapeutic alternatives with large variation in time on market; (2) preference for evidence synthesis methods (e.g., network meta-analysis, indirect treatment comparison); (3) planned best practices by which CMS will evaluate the quality of comparative effectiveness studies; and (4) the planned comprehensive approach to evaluating how the selected drug and treatment alternatives impact patients and the health system, which will require a comparison of not only regulatory endpoints but also patient reported outcomes and broader measures of impact across patients and their informal caregivers (i.e., adherence, productivity, quality of life); and (5) clear information on how CMS will compare and synthesize data across outcomes that highlight important differences in the impact of treatments that are not well suited for formal evidence synthesis given: data missingness, heterogeneous populations, variations in outcome definition and imbalanced effect modifiers across studies and populations. When updating the definition of requested CMS data, we recommend that CMS also seek to align their approach with other comparative effectiveness research organizations (e.g., Patient-Centered Outcomes Research Institute (PCORI)).

Unmet Need: CMS' proposed definition of unmet need is simultaneously restrictive and vague. CMS should develop a more robust definition for unmet need that provides information beyond 'very limited or no other treatment options.' For example, how will CMS define unmet need in cancers without a cure, or chronic diseases with high levels of disability? When updating the definition of unmet need, CMS should consider the impact of the definition on vulnerable patients and health equity. Further, CMS should seek to align the definition of unmet need with long-standing definitions used by the FDA to ensure alignment on how the US government will support development of future medicines that address unmet need. To this end, we recommend CMS adopt the following standards for "unmet medical need":

- A product approved to meet an unmet medical need as defined by FDA in its 2014 Guidance; OR
- A product that treats patient group previously unresponsive to or ineligible for currently available treatments;
  OR
- A product targeting a disease state affecting a disproportionate share of vulnerable patients (i.e., socially vulnerable or disadvantaged, low socioeconomic status, disabled).

Cost of Therapeutic Alternatives: In Question 41, CMS asks respondents to "[p]lease provide current costs of . . . existing therapeutic alternatives (if known)." We recognize that the statute contemplates that

[9] National Center for Biotechnology Information. Definition and Resources on Clinical Outcome Assessments. Accessed: https://www.ncbi.nlm.nih.gov/books/NBK338448/def-item/glossary.clinical-outcome-assessment/

CMS will collect information regarding "the costs of . . . existing therapeutic alternatives." However, we do not believe it is appropriate to consider these costs for purposes of identifying therapeutic alternatives. Instead, we recommend that CMS clarify that the sole function of collecting this information is to identify the starting point for the negotiation process, which CMS has proposed will begin with the price of the selected drug's therapeutic alternatives.

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We welcome the opportunity to discuss these comments with you further and address any questions you may have. Please reach out to me or Valerie Reynolds (reynolds.valerie@gene.com) at any time.

Sincerely,

David Burt
Executive Director
Federal Government Affairs
david.burt@gene.com

cc: Lara Strawbridge
IRARebateandNegotiation@cms.hhs.gov

May 22, 2023

Via Electronic Filing: *http://www.regulations.gov*

William Parham
CMS, Office of Strategic Operations and Regulatory Affairs
Division of Regulations Development
Attention: CMS-10847, OMB, 0938-NEW
Room C4-26-05
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)

Dear Mr. Parham:

Gilead Sciences, Inc. (Gilead) appreciates this opportunity to submit these comments in response to the Centers for Medicare & Medicaid Services' (CMS') *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act* (ICR), including the Federal Register Notice, Supporting Statement–Part A, and ICR Form (CMS-10847, OMB, 0938-NEW).[1]

Gilead is a research-based biopharmaceutical company that discovers, develops, and commercializes innovative medicines in areas of unmet medical need. We endeavor to transform and simplify care for people with life-threatening illnesses around the world. Our portfolio of products and pipeline of investigational drugs includes treatments for HIV/AIDS, liver diseases, cancer, and inflammatory and respiratory diseases. Our portfolio of marketed products includes a number of category firsts, including complete treatment regimens for HIV infection available in a once-daily single pill, the first oral antiretroviral pill available to reduce the risk of acquiring HIV infection in certain high-risk adults, and the first hepatitis C virus (HCV) treatment to provide a complete regimen in a single tablet. Gilead is committed to ensuring that people have access to our medicines.

We appreciate the efforts of CMS to solicit comments on a proposed form to collect data regarding drugs selected under the Inflation Reduction Act (IRA) "Medicare Drug Price Negotiation Program" (MFP Program). The comments that follow are intended to further build on the comments of our trade associations, the Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO). In addition, Gilead discussed our concerns and recommendations related to the factors CMS will consider in

[1] *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act, Supporting Statement–Part A*, 88 Fed. Reg. 16,983 (Mar. 21, 2023). *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847; *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act, ICR Form* (Mar. 21, 2023). *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847 (hereinafter "ICR Form").

determining the "Maximum Fair Price" (MFP) in comments filed in response to CMS' initial guidance (Initial Guidance) regarding the implementation of the MFP Program.[2] While we refer to some of our positions in response to the Initial Guidance in this letter, we do not reiterate all of those comments in this letter. We ask that CMS consider these letters in tandem for the full extent of our recommendations.

Our specific comments on the ICR requests can be summarized briefly as follows:

- The Value-Related Factors Set Forth in SSA § 1194(e)(2) Should Be Weighted More Heavily than the Cost-Related Factors in SSA § 1194(e)(1). In general, we encourage CMS to more heavily weigh the value-related factors set forth in Section 1194(e)(2) of the Social Security Act (SSA) compared to cost-related drug development factors in Section 1194(e)(1). Prioritizing cost-based factors could lead to prices that reduce incentives for investment in biopharmaceutical research, especially for diseases with the greatest unmet need, as those diseases may require the most difficult research or represent smaller populations. Prioritizing cost-based factors could also result in research and development (R&D) that is less efficient, leading to fewer and slower scientific advances. Moreover, the proposed reporting requirements for the cost-related factors in Section 1194(e)(1) are highly complicated and burdensome for manufacturers to identify, track, and submit. We ask that CMS significantly reduce the number of data elements collected for the Section 1194(e)(1) factors, particularly the R&D costs and pricing metrics, and utilize existing metrics and sources of information where possible.

- The Proposed R&D Metrics Do Not Capture the Full Scope of Investment Necessary for Drug Development and Will Be Challenging, if Not Impossible, for Manufacturers to Report with Precision. The ICR data elements do not accurately reflect the full scope of investment in the drug development process, which often builds on discovery and study of hundreds if not thousands of potential molecules. Given the nature and challenges of R&D, we ask that CMS permit manufacturers to report all R&D costs in a drug category that supported a drug's discovery, for both approved and unapproved indications. Additionally, the ICR requests unnecessarily extensive R&D data, which goes beyond the scope of the statutory language, and in many cases will be challenging or impossible for manufacturers to identify and report with precision. Given these concerns about the R&D metrics being too limited in scope while also being high burden, CMS should rely on broad publicly reported R&D metrics such as those in Securities and Exchange Commission (SEC) filings and allow manufacturers to use reasonable assumptions to allocate a percentage of total R&D costs to the R&D that led to a drug's approval and supports ongoing discovery.

- Considering Prior Federal Financial Support Has the Potential to Reduce Incentives for Future Collaborations in Research. CMS' plan to adjust the preliminary MFP Program price downward based on prior federal financial support does not align with the shared goal of advancing biopharmaceutical innovation. The federal government primarily supports basic science, and desires to license promising research to companies to further develop and

[2] Memorandum from Meena Seshamani, M.D., Ph.D., CMS Deputy Administrator and Director of the Center for Medicare to Interested Parties, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191–1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (March 15, 2023), *available at* https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf (hereinafter "Program Initial Guidance").

commercialize products. Such transactions are an important aspect of biopharmaceutical development in the U.S, and CMS' proposed approach would disincentivize future collaboration between government agencies and pharmaceutical manufacturers. Moreover, adjusting the MFP Program price downward based on prior federal financial support fails to recognize the significant investments manufacturers make in drug development with no guarantees of success.

- Manufacturers Should Not Be Penalized for Intellectual Property Rights Intended to Incentivize Research and Development. Applying a downward adjustment to the preliminary price on the basis of remaining patents and exclusivity will greatly disincentivize ongoing R&D and it directly conflicts with the purpose of those protections—incentivizing innovation. Drug development is a continuous process that involves constant innovation and multiple improvements for each product. The setting of any MFP before a product's patents and exclusivities expire has great potential to undermine patent incentives to undertake risky investments in such ongoing R&D; penalizing inventions that result in patents when determining an initial offer would only further disincentivize such risk taking by manufacturers. CMS should instead adjust the preliminary price upward to reward new data and/or expansion of indications to incentivize scientific breakthroughs.

- To Reduce the Burdens on Manufacturers and Help Ensure CMS Receives Consistent and Accurate Data, Existing Price Reporting Metrics Should be Used and the Reporting Period Should be Reduced. Instead of creating new price reporting metrics as proposed in the ICR, CMS should use existing, established, and reliable metrics to ensure that it has access to consistent and accurate data regarding market prices. The introduction of new metrics related to U.S. commercial average net unit price and manufacturer average net unit price to Part D Plan sponsors imposes significant burdens on manufacturers and may result in inconsistent and unreliable data. To reduce the significant reporting burden placed on manufacturers due to the volume of data requested and the very short reporting period, CMS also should limit its requests to the one-year period prior to a drug's selection. If CMS believes it is necessary to collect pricing information across multiple calendar years, we suggest that the agency ask manufacturers to report five or six quarters of data.

- 340B Sub-Ceiling Prices and FSS Voluntary Discounts Should Not Inform the MFP Determination. CMS should not collect or use 340B Prime Vendor Program Prices, other 340B sub-ceiling prices, or voluntary discounts to Federal Supply Schedule (FSS) purchasers in determination of the MFP, as doing so would strongly disincentivize such voluntary manufacturer discounts.

- The ICR Must Provide Manufacturers an Opportunity to Submit Sufficient Information to Provide CMS with a Complete and Holistic Understanding of the Clinical and Societal Value of a Therapy. As noted above, Gilead strongly believes that clinical and societal value should be heavily weighted in MFP determinations. However, the ICR proposes unworkable word counts for the collection of data and information related to the value of a selected drug that will not allow for a complete submission of information. To ensure CMS is able to assess the full value of a drug, it should expand the reporting fields to allow manufacturers to provide a comprehensive set of evidence that provides the full picture of the selected drug's clinical and societal value.

- The Proposed Thirty (30) Day Reporting Window is Too Short. We also believe that a thirty (30) day window for reporting all of the ICR data elements to CMS after a manufacturer receives notification of drug selection is far too short to collect information and submit a robust response. We ask that CMS extend the period to at least ninety (90) days, given the amount of data requested.

I. The Value-Related Factors Set Forth in SSA § 1194(e)(2) Should Be Weighted More Heavily than the Cost-Related Factors in SSA § 1194(e)(1).

As a threshold matter, we strongly encourage CMS to place greater weight on the value-related factors set forth in Section 1194(e)(2) and less weight on the price and cost-related factors in Section 1194(e)(1) of the Social Security Act. We are concerned that the vast majority of the proposed data submission requirements in the ICR relate to factors such as pricing, costs of R&D, costs of production and distribution, and other cost-related factors for the selected drug. Even if each cost-related factor is given a small weight, the overall weight of these factors in the MFP determination could be significant.

Gilead prices our drugs based on the drug's value to patients and society. This approach centers on an understanding that the value medicines bring will be recognized by the health care system and provide an opportunity to support the discovery of next-generation medicines. This is critical because about ninety percent (90%) of development programs ultimately fail,[3] and successful drugs must sustain a manufacturer's total R&D investment. However, tying a medicine's price to an assessment of its development costs and related factors does not reward success or reflect a drug's full value, and "may fail to stimulate new drug development in areas where it is most needed."[4] It may also result in inefficient R&D, as more R&D spending may prevent larger downward adjustments in price.

Prioritizing the cost-related factors in establishing an MFP will not ensure that prices reflect the benefits that medicines bring to patients and society. This, combined with the fact that the MFP is set so long before patent expiry for many small molecule medicines, has the potential to dramatically change incentives for future manufacturer R&D across all research pipelines (not just for the selected drug at issue). Setting prices that do not reflect value could reduce investment in small molecule medicines—including many drugs to treat infectious diseases and targeted cancer therapies—and even reduce investment in medicines overall.[5] This is because cost-based pricing reduces the potential for the value of a medicine to be reflected and instead essentially ensures that establishment of an MFP will have a similar impact to generic entry. Thus, to preserve the incentives needed for manufacturers to invest in R&D and address critical areas of unmet need, value should be weighted far more heavily than the cost-related factors.

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[3] *See, e.g.*, Duxin Sun et al., *Why 90% of Clinical Drug Development Fails and How to Improve It?*, ACTA PHARMACEUTICA SINICA B, 3049 (July 2022), *available at* https://www.sciencedirect.com/science/article/pii/S2211383522000521 (explaining that ninety percent (90%) of clinical drug development fails, despite implementation of many successful research strategies over time).

[4] Peter J. Neumann et al., *Drug-Pricing Debate Redux–Should Cost-Effectiveness Analysis be Used Now to Price Pharmaceuticals?*, 385 NEW ENG. J. MED., 1923 (Nov. 18, 2021), *available at* https://www.nejm.org/doi/full/10.1056/NEJMp2113323.

[5] Dana Goldman, et al., *Mitigating the Inflation Reduction Act's Adverse Impacts on the Prescription Drug Market*. (2023), *available at* https://healthpolicy.usc.edu/research/mitigating-the-inflation-reduction-acts-potential-adverse-impacts-on-the-prescription-drug-market/.

Moreover, as described further below, the proposed reporting requirements for the cost-related factors in Section 1194(e)(1) are highly complex, unclear, and burdensome for manufacturers. Because of the challenges manufacturers will face in reporting this information, these requirements may yield data that is inconsistent and of variable quality by manufacturer and product, limiting its utility for CMS. Accordingly, we ask that CMS significantly reduce the number of data elements collected for the Section 1194(e)(1) factors, particularly the R&D costs and pricing metrics, and utilize existing metrics and sources of information where possible.

II. The Proposed R&D Metrics Do Not Capture the Full Scope of Investment Necessary for Drug Development and Will Be Challenging, if Not Impossible, for Manufacturers to Report with Precision.

A. The R&D Metrics CMS Has Proposed for Manufacturer Submission are Overly Narrow.

The proposed R&D data elements do not accurately reflect the full scope of investment necessary in developing a drug. As noted above, about ninety percent (90%) of drug development programs fail.[6] This statistic only includes drug candidates that have already advanced to phase 1 clinical trials, and does not even include drug candidates in the preclinical stages.[7]

The significant financial risks that manufacturers face in investing in drug R&D are not captured by the narrow metrics set forth in the ICR. For example, Question 5 of the ICR requires manufacturers to report the costs of failed or abandoned products related to the selected drug, and defines "failed or abandoned product costs" to include "a sum of the portion of direct basic pre-clinical research costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and a portion of direct post-IND costs for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval." While we appreciate that CMS is proposing that manufacturers be allowed to report costs related to failed pre-clinical research, the limitation to costs for drugs with the same active moiety / active ingredient or mechanism of action is overly narrow and will not capture all of the resources used to generate the knowledge that leads to one drug.

Since its founding decades ago, Gilead has invented, researched, and developed many new antiviral compounds. Gilead scientists continually work to invent new small molecules and biologics in order to generate an expansive library of diverse technology platforms that can be accessed and tested against new pathogens. In the field of antivirals, each discovery and study of a potential molecule—even if it does not succeed against a specific target or pathogen, or result in FDA approval—contributes important knowledge that informs future discovery.

HIV R&D and innovation are examples of the challenges and iterative nature of R&D. There have been over 3,000 clinical trials of potential HIV treatments since 1990, but only fifty-seven FDA-approved medicines. These fifty-seven drugs work in different ways and have been combined into different regimens because people living with HIV have unique and diverse needs.[8]

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[6] *See, e.g.,* Sun et al., *supra* note 5.
[7] *Id.*
[8] Kristen Axelsen, et al. *Assessing the Implications of Centralized Drug Price Setting to Investment in Clinical Development in HIV Treatments, A Study for Gilead Sciences* (2021) *available at* https://www.crai.com/insights-

For some regimens used today, R&D for component drugs may have been initiated over thirty years ago, while innovative components have been developed more recently. Each of the failed trials in HIV generated knowledge that contributed to future R&D. Gilead, for example, recently received approval for Sunlenca, a first-in-class long-acting capsid inhibitor for highly-treatment experienced patients.[9] This discovery of a new mechanism of action in HIV was possible only because of the knowledge Gilead has built over time in HIV, and came after thousands of potential antiretroviral agents—including both capsid inhibitors and other types of compounds—were evaluated and failed over many years.

Accordingly, CMS should permit manufacturers to report all R&D investment, including pre-clinical research costs, in a drug category (*e.g.*, HIV medicines) that supported discovery of the selected drug. This should include all failed R&D and apply to both FDA approved indications and unapproved indications. The example of remdesivir below highlights why it is important to consider R&D on both approved and unapproved indications.

B. Manufacturers Face Significant Challenges in Accurately Identifying, Tracking, and Collecting R&D Costs Associated with a Particular Drug.

The ICR requests highly detailed R&D data, extending significantly beyond the scope of the statutory language, some of which is inaccessible to manufacturers. Again, Gilead's work to develop antivirals illustrates the complexity of R&D and the challenges with identifying, tracking, and collecting R&D costs over time for any particular drug.

An example of this is remdesivir, an FDA-approved antiviral treatment for patients with COVID-19.[10] Gilead had already invested in clinical trials assessing remdesivir's safety and broad-spectrum activity prior to the COVID-19 pandemic. By February 2020—a full month before the World Health Organization (WHO) declared a pandemic—Gilead began clinical trials of remdesivir in COVID-19, and by May 2020 the FDA authorized remdesivir's use under an Emergency Use Authorization (EUA).[11] It received full FDA approval in October 2020. Gilead spent over $1 billion in 2020 alone in developing and manufacturing remdesivir for treatment of COVID-19. While we are able to measure these discrete R&D expenditures in 2020, this does not come close to measuring all of the R&D investment that went into developing remdesivir, including the investment in developing remdesivir over the prior decade or more.

The research that led to the invention of remdesivir began as early as 2009, with research programs under way for hepatitis C virus (HCV) and respiratory syncytial virus (RSV). This research was exclusively funded by Gilead. Following the invention of remdesivir, we continued

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events/publications/assessing-the-implications-of-centralized-drug-price-setting-to-investment-in-clinical-development-for-hiv-treatments/.

[9] *FDA Approves New HIV Drug for Adults with Limited Treatment Options.* FDA News Release (Dec. 22, 2022), *available at* https://www.fda.gov/news-events/press-announcements/fda-approves-new-hiv-drug-adults-limited-treatment-options (announcing FDA's approval of Sunlenca, "a new type of antiretroviral medication for adult patients living with [HIV-1], whose HIV infections cannot be successfully treated with other available treatments due to resistance, intolerance, or safety considerations.").

[10] FDA Approves First Treatment for COVID-19, FDA News Release (Oct. 22, 2020), *available at* https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-covid-19.

[11] Gilead, *Gilead Sciences Statement on Access to Remdesivir Outside of Clinical Trials* (Mar. 22, 2020) *available at* https://www.gilead.com/news-and-press/company-statements/gilead-sciences-statement-on-access-to-remdesivir-outside-of-clinical-trials.

to explore various uses for the compound, including identifying its activity against coronaviruses in 2013 and confirming its antiviral activity against various viruses, including RSV, SARS, MERS, Marburg and Ebola. Gilead research scientists have explored the compound for multiple potential uses to help address urgent and unmet medical needs around the world.[12]

As the history of remdesivir demonstrates, R&D for one drug may be highly complex and multi-faceted, with multiple trials occurring at different times in different indications and patient populations, across multiple internal teams and external research sites. Gilead does not have systems in place now to track spending with the specificity that would be required to respond fully and accurately to the proposed R&D metrics, and we certainly did not ten or twenty years ago when related R&D may have been occurring. Additionally, Gilead itself has grown dramatically over the past couple of decades, with under 300 employees in 1998 and more than 16,000 today. Given these challenges, there will be significant variation in quality and consistency of the data reported to CMS across companies and products. Different companies are going to report these metrics in different ways and with varying levels of precision. This means that these metrics will have low utility to CMS, yet high levels of burden to manufacturers.

To address the concerns above that the proposed R&D metrics (1) do not fully capture the R&D related to a drug's discovery and (2) are highly burdensome and imprecise, we ask that CMS only require reporting of comprehensive R&D metrics already reported by manufacturers in other contexts. For example, manufacturers could utilize SEC filings that include total R&D spend and use reasonable assumptions, similar to those that manufacturers use for the Medicaid Drug Rebate Program (MDRP) and Average Sales Price (ASP) calculations, to allocate a percentage of total R&D costs to the efforts that led to approval and ongoing development of a selected drug.

III. Considering Prior Federal Financial Support Has the Potential to Reduce Incentives for Future Collaborations in Research.

Section 60.3 of CMS' Initial Guidance on the Program provides that when considering prior federal financial support, "CMS intends to consider the extent to which the Primary Manufacturer benefited from Federal financial support. For example, CMS may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from Federal sources."[13] Gilead opposes this downward adjustment based on federal financial support, because it will likely inhibit future collaborations in drug development research.

In considering information about prior federal financial support provided to a manufacturer, it is important for CMS to understand the pharmaceutical industry's role in the U.S. drug research ecosystem. A large majority of R&D in the U.S. is privately funded.[14] The federal government primarily supports basic science, and desires to license promising research to companies to further develop and commercialize products.[15] Collaboration with entities such as

[12] *See, e.g.*, Gilead, *Development of Veklury*, *available at* https://www.gilead.com/-/media/files/pdfs/medicines/covid-19/veklury/veklury-remdesivir-development-backgrounder.pdf.
[13] *See* Program Initial Guidance at 53.
[14] *See, e.g.*, Duane Schulthess, et al., *The Relative Contributions of NIH and Private Sector Funding to the Approval of New Biopharmaceuticals*, 57 THER. INNOV. REGUL. SCI. 160 (2022), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9440766/ 5 corrected by 57 THER. INNOV. REGUL. SCI. 170 (Sep. 16, 2022) *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9755103/.
[15] *Id.*

the National Institute of Health (NIH) can be a key part of drug development, as shown by the successful medicines that have come from these partnerships. For example, manufacturers often undertake the significant costs of translational R&D required to advance basic science research by entities such as NIH into safe and effective treatments available to patients.[16]

Penalizing manufacturers for these types of partnerships by reducing the drug's MFP based on prior federal financial support will disincentivize future collaboration between manufacturers and research entities such as NIH, which could decrease the likelihood of future NIH research ultimately being developed into medicines. Manufacturers make significant additional investments to take basic science through clinical development all the way to product launch, with no guarantees of success. CMS should revise its Initial Guidance so that manufacturers are not penalized for receiving prior federal financial support when the Program sets the drug's MFP. This is both fair to manufacturers who make substantial investments with no guarantees of success and promotes collaboration between manufacturers and government entities such as NIH, which is a critical aspect of the U.S. drug research ecosystem.

IV. Manufacturers Should Not Be Penalized for Intellectual Property Rights Intended to Incentivize Research and Development.

Gilead remains concerned that by significantly shortening the time period in which a manufacturer may determine its own price to as few as *nine* years for drugs approved under a New Drug Application (NDA) and *thirteen* years for biological products approved under a Biologics License Application (BLA), the MFP Program has the potential to undermine the incentives created by the patent system.[17] This approach is particularly troubling given that HIV treatments generally are approved under NDAs and therefore subject to the Program four years sooner than would be a comparable biological product.[18]

Yet, as currently proposed, CMS "intends to consider the length of the available patents and exclusivities before the drug may no longer be single source" and "if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price *downward*."[19] Using pending and approved patents, regulatory exclusivity periods, and active and pending FDA applications and approvals as factors that may result in a downward adjustment to the preliminary price will only further disincentivize post-approval R&D that could lead to a patent or regulatory exclusivity—while penalizing manufacturers for relying on long-established intellectual property rights designed to promote scientific and medical breakthroughs.[20] Patents signify and are intended to reward innovation, and manufacturers should not be punished for identifying new uses and applications of their products.

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[16] *See* Vital Transformation, *Who Develops Medicines? An Analysis of NIH Grants* (2021), *available at* https://vitaltransformation.com/2021/05/who-develops-medicines-an-analysis-of-nih-grants/

[17] *See* SSA §§ 1192(e)(1)(A)(ii), (B)(ii).

[18] *Compare* SSA § 1192(e)(1)(A)(ii) ("A drug . . . for which, as of the selected drug publication date with respect to such initial price applicability year, at least 7 years will have elapsed since the date of such approval[.]") *with id* § 1192(e)(1)(B)(ii) ("A biological product . . . for which, as of the selected drug publication date with respect to such initial price applicability year, at least 11 years will have elapsed since the date of such licensure[.]").

[19] Program Initial Guidance at 53 (emphasis added).

[20] For instance, Article I of the U.S. Constitution provides for Congress "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." U.S. Const., art. I, § 8, cl. 8.

Moreover, the existing intellectual property landscape already balances the need to preserve, promote, and incentivize innovation with an abbreviated path for generic drugs through the Drug Price Competition and Patent Term Restoration Act (commonly referred to as the Hatch-Waxman Act). CMS should not disturb the carefully crafted regime enacted by Congress almost four decades ago, which has established an active generics market for drugs following patent expiry while still ensuring that the United States remains a leader in biopharmaceutical R&D.

CMS' proposed approach will exacerbate the impact of the IRA on the incentives and resources of manufacturers to invest in the development of innovative drugs that address unmet medical needs. This impact is particularly concerning for HIV therapies. As manufacturers develop novel HIV medicines, these innovations over time form important building blocks toward a cure for HIV. If CMS uses such breakthroughs to disincentivize innovation in the HIV therapeutic area, the negative ramifications on innovation that Gilead believes is critical to ending the HIV epidemic could be profound. Accordingly, CMS should adjust the preliminary price upward to reward new data and/or expansion of indications and to incentivize scientific breakthroughs.

V. To Reduce the Burden on Manufacturers and Help Ensure CMS Receives Consistent and Accurate Data, Existing Price Reporting Metrics Should be Used and the Reporting Period Should be Reduced.

CMS proposes the reporting of several new price reporting metrics in Section G of the ICR, which will impose significant burdens on manufacturers. While many of the metrics are well defined and familiar to CMS and the industry, CMS proposes adding two new categories, as well as variations of each: (1) U.S. commercial average net unit price; and (2) Manufacturer average net unit price to Part D Plan sponsors.[21] For both of these price metrics, CMS seeks the price with patient assistance programs, without patient assistance programs, and the "best" price (*e.g.*, "the lowest U.S. commercial average net unit price offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S." and "the lowest manufacturer average net unit price to Part D Plan sponsors offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any Part D plan sponsor").[22] These new metrics introduced in the ICR are not well defined, which will not only create unnecessary burdens on manufacturers but

[21] *See* ICR Form Questions 31, 32 (Commercial Average Net Unit Price); 33, 34 (Manufacturer Average Net Unit Price to Part D Plan Sponsors); *see also id.* at. 25-26 (definitions of U.S. commercial average net unit price; U.S. commercial average net unit price─without patient assistance program; U.S. commercial average net unit price─best; manufacturer average net unit price to Part D plan sponsors; manufacturer average net unit price to Part D Plan sponsors─without patient assistance program; and manufacturer average net unit price to Part D Plan sponsors─best).

[22] *See id.* at 26 (defining "U.S. commercial average net unit price─ best" as the "the lowest U.S. commercial average net unit price offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S.;" and "Manufacturer average net unit price to Part D Plan sponsors─best" as the "the lowest manufacturer average net unit price to Part D Plan sponsors offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any Part D plan sponsor. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any purchasers.").

may also result in unreliable data given the likelihood of inconsistent reporting across manufacturers.

Instead of these two new categories of pricing metrics (and all the permutations therein), Gilead urges CMS to utilize only those metrics that manufacturers currently report to the government, such as Best Price and Average Manufacturer Price (AMP), because they have been defined through the regulatory process—including regulations and hundreds of pages of preamble guidance—which helps ensure that CMS receives consistent and reliable data across manufacturers. Moreover, use of existing price reporting metrics that are already available to CMS will allow the Agency to leverage the department's familiarity and experience with each of the existing metrics. Additionally, manufacturers are generally required to report gross revenue information to the SEC on a quarterly basis for their top selling medicines. CMS should leverage this existing data rather than collecting new categories of information for gross revenue and net revenue.

The lack of clarity regarding the other new reporting metrics also has the potential to result in ambiguous data that fails to present CMS with accurate information concerning the selected drug. For example, the ICR would require reporting of the "total costs of the acquisition of the NDA(s)/BLA(s) of the selected drug," which would "[i]nclude costs of previously approved or future NDA/BLA(s) of other drugs and biological products if these other drugs and biological products were part of the same acquisition as the previously approved or future NDA/BLA(s) of the selected drug." Manufacturers would also be required to "provide a proportional allocation of the total acquisition costs reported … in situations where the total acquisition costs of the approved or future NDA/BLA(s) of the selected drug included costs other than for acquisition of the selected drug." Although CMS proposes allowing manufacturers to describe the methodology used to allocate the total acquisition costs for the selected drug, it does not specify how the total acquisition costs for an NDA or BLA should be split among different existing and future therapies derived from the same acquisition. CMS should allow manufacturers to report a weighted allocation based on an expected volume of sales for each applicable product in the initial price applicability year for the selected drug.

In addition, throughout the ICR, CMS asks manufacturers to provide quarterly data for the most recent five years, where applicable.[23] To reduce the significant reporting burden placed on manufacturers in light of the volume of data requested and the very short reporting period—particularly if CMS finalizes is proposal to require new and untested pricing metrics—CMS should limit its requests to the one-year period prior to selection. Requiring up to twenty quarterly data points for each applicable question imposes significant burden on manufacturers while providing CMS with little to no additional insight. Instead, limiting reports to quarterly data for the twelve-month period preceding a drug's selection will provide CMS with a sufficient and workable volume of data over the most relevant period of time without collecting stale or outdated information. Because manufacturers will be required to report information on a quarterly basis, one year of data would also give CMS pricing trend information. If CMS believes it is necessary

[23] *See id.* at 28-38 (ICR Questions 19 (Wholesale Acquisition Cost Unit Price); 21 (340B Ceiling Price); 23 (340B Prime Vendor Program Price); 25 (Medicaid Best Price); 27 (Federal Supply Schedule Price); 29 (Big Four Price); 31 (U.S. Commercial Average Net Unit Price); 33 (Manufacturer Average Net Unit Price to Part D Plan Sponsors); 35 (Quarterly Total U.S. Gross and Net Revenue); 37 (Quarterly Total U.S. Unit Volume)).

to collect pricing information across multiple calendar years, we suggest that the agency could ask manufacturers to report five or six quarters of data.

VI. 340B Sub-Ceiling Prices and FSS Voluntary Discounts Should Not Inform the MFP Determination.

Gilead strongly objects to the proposal in Question 23 to collect 340B Prime Vendor Program Prices. Reporting sub-ceiling 340B prices for consideration in the MFP determination will disincentivize manufacturers from providing these voluntary prices in the future. Manufacturers may provide sub-ceiling discounts to 340B covered entities.[24] These discounts support the intent of the 340B program: improving low income and medically underserved patients' ability to affordably access their prescribed medicines. Considering these voluntary discounts in determining the MFP applicable to the entire Medicare program, however, could magnify their cost and strongly discourage them.

Such a result would run counter to a longstanding intent by Congress to *encourage* 340B sub-ceiling prices by manufacturers, as demonstrated by Congress' excluding them from pricing metrics. The 340B statute specifically provides that "[n]othing . . . shall prohibit a manufacturer from charging a price for a drug that is lower than the" 340B ceiling price,[25] and the Medicaid rebate statute excludes "any price" to 340B entities from Best Price.[26] In its regulations, CMS also has appropriately excluded "any prices" (including sub-ceiling prices) offered to 340B covered entities from Best Price.[27] Nothing in the IRA suggests that Congress intended to undermine these longstanding incentives. CMS thus should take a similar approach to the one it has taken in the MDRP context and refrain from collecting 340B Prime Vendor Program Prices (or any other 340B sub-ceiling prices) through the data collection form or considering them in the MFP determination process.

Similarly, manufacturers may offer voluntary discounts to FSS purchasers that are below the Big 4 or Dual FSS price that is negotiated with the Department of Veterans Affairs (VA). Like 340B sub-ceiling discounts, Congress and CMS have excluded these FSS voluntary discounts from the Medicaid Best Price determination.[28] To avoid disincentivizing manufacturers from offering voluntary discounts to FSS purchasers that are below the Federal Ceiling Price (FCP) for the Big 4 agencies or the negotiated Dual FSS price for other government agencies, CMS should adopt the same approach with respect to the MFP determination. Specifically, CMS should clarify that: (1) the "Federal supply schedule (FSS) price" is the FSS price negotiated with the VA for other government agencies, exclusive of any temporary price reductions (TPRs) or blanket purchase agreements (BPAs); and (2) the "Big Four price" is the FCP determined in accordance with 38 U.S.C. § 8126 and agreed to by the manufacturer on Addendum A to the VA Master Agreement.

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[24] *See* K. Mulligan. *The 340B Drug Pricing Program: Background, Ongoing Challenges and Recent Developments. USC Schaeffer,* (2021), *available at:* https://healthpolicy.usc.edu/research/the-340b-drug-pricing-program-background-ongoing-challenges-and-recent-developments/.
[25] 42 U.S.C. § 256b(a)(10).
[26] SSA § 1927(c)(1)(C)(i)(I).
[27] 42 C.F.R. § 447.505(c)(2); 81 Fed. Reg. 5170, 5257 (Feb. 1, 2016) ("[A]ny prices charged by manufacturers and paid for by covered entities shall be excluded from best price. Furthermore, we believe that this change clarifies that manufacturers may exclude any prices offered at or below the 340B ceiling price (subceiling prices).") *available at* https://www.federalregister.gov/documents/2016/02/01/2016-01274/medicaid-program-covered-outpatient-drugs.
[28] SSA § 1927(c)(1)(C)(i)(I).

CMS also should not require reporting by manufacturers of any other metrics regarding voluntary prices to Federal agencies.

VII. The ICR Must Provide Manufacturers an Opportunity to Submit Sufficient Information to Provide CMS with a Complete and Holistic Understanding of the Clinical and Societal Value of a Therapy.

Section H of the ICR voluntarily seeks evidence regarding comparative effectiveness of a drug to "Alternative Treatments" and evidence of unmet need. In responding to these factors, manufacturers must be permitted to provide CMS with a full understanding of the clinical and societal value of a therapy. We are concerned that the opportunity to provide a complete set of data and evidence in response to Questions 39 through 43 will be severely limited by the proposed word counts in the ICR. In addition, as discussed below, a thirty (30) day window for reporting the ICR data elements after notification of drug selection is far too short to collect the necessary information and submit a robust response.

The ICR calls for responses no longer than 1,000 words to address unmet need and 3,000 words to address therapeutic impact and comparative effectiveness. These word limits severely constrain a manufacturer's ability to provide key information to CMS. By the time a drug approved under an NDA is selected under the MFP Program, it will have been approved at least seven years ago; a biological product will have been licensed no less than eleven years at the time of selection.[29] At this point, a tremendous volume of data and real-world evidence will exist. For a drug with multiple indications and uses in different patient subpopulations, it would be impossible to fully answer these questions within the proposed confines—depriving CMS of critical information. For comparison, Gilead regularly compiles and submits information in Academy of Managed Care Pharmacy (AMCP) dossiers to health technology assessment organizations and payers. These dossiers are often hundreds of pages in length and contain detailed evidence to allow for an assessment of the safety, effectiveness, efficacy, and value of new therapies.[30] CMS should significantly expand the reporting fields in Section H to allow manufacturers to provide a comprehensive set of evidence that provides the full picture of the selected drug's clinical and societal value.

In addition, as discussed in Gilead's comment letter regarding CMS' Initial Guidance, Gilead urges CMS to clarify that the selection of Alternative Treatments should be based *exclusively* on clinical appropriateness, rather than on the cost of therapy.[31] Clinical appropriateness should be determined through review of clinical guidelines, input from clinical experts, manufacturers, and providers, and other related methods. It is thus crucial that stakeholders have a meaningful opportunity to provide such input to CMS to inform the Agency's determination.

Gilead supports CMS' intention to allow all stakeholders to submit data and evidence in response to these factors. In doing so, CMS should also commit to providing full transparency into

[29] *See* SSA §§ 1192(e)(1)(A)(ii), (B)(ii).
[30] *See, e.g., AMCP Format for Formulary Submissions, Guidance on Submission of Pre-approval and Post-approval Clinical and Economic Information and Evidence*, Academy of Managed Care Pharmacy (2020), *available at* https://www.amcp.org/sites/default/files/2019-12/AMCP_Format%204.1_1219_final.pdf.
[31] *See* Letter from Rekha Ramesh, Vice President, Policy, Gilead Sciences, Inc. to Dr. Meena Seshamani, CMS Deputy Administrator & Director of Center for Medicare, CMS 15 (Apr. 14, 2023).

the information that was submitted and whether and how CMS considered it in determining its initial offer. To support public trust in the MFP Program, CMS should fully explain the basis for its initial price—including which therapies it considered to be Alternative Treatments, and the impact of those drugs on CMS' decision making.

VIII. The Proposed Thirty (30) Day Reporting Window is Too Short.

Lastly, we believe that a thirty (30) day window for reporting the ICR data elements to CMS after a manufacturer receives notification of selection of its drug for the MFP Program is far too short to collect information and submit a robust response. This short window adds to the significant reporting burden placed on manufacturers and increases the potential for inconsistent or inaccurate responses across manufacturers. We ask that CMS extend the period to at least ninety (90) days, given the amount of data requested. Providing adequate time for manufacturers to collect and report this data will help facilitate accurate and reliable submissions and support the overall integrity of the MFP Program.

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Gilead hopes CMS will incorporate these suggestions when it revises the Information Collection Request Form for Negotiation Data Elements with a goal of minimizing potential negative impacts on biopharmaceutical innovation and patient access to medicines. If you have any questions, please do not hesitate to contact Russ Montgomery at russ.montgomery@gilead.com.

Sincerely,

Rekha Ramesh
Vice President, Policy
Government Affairs and Policy
Gilead Sciences, Inc.

GSK Comment Letter

Response to Information Collection Request for Negotiation Data Elements of the Inflation Reduction Act

May 22, 2023

Via electronic submission: Regulations.gov

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attention: PO Box 8016

RE: Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)

Dear Deputy Administrator Seshamani:

GSK appreciates the opportunity to comment in response to the Centers for Medicare & Medicaid Services (CMS or the Agency) Information Collection Request (ICR or the ICR) for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (IRA or the Act), including the Federal Register Notice, Supporting Statement – Part A, and ICR Form (CMS-10847, OMB, 0938-NEW).

GSK is a global biopharmaceutical company with the ambition and purpose to unite science, technology, and talent to get ahead of disease together. We seek to prevent and treat disease with vaccines, specialty, and general medicines. Our global specialist HIV company, ViiV Healthcare, is fully dedicated to delivering advances in prevention, treatment, and care for people living with HIV/AIDS.

GSK supports policy solutions that transform our U.S. healthcare system to one that rewards innovation, improves patient outcomes, and achieves higher value care. GSK is a member of and endorses the comments of the Pharmaceutical Research & Manufacturers of America (PhRMA) and the Biotechnology Innovation Organization (BIO) on this ICR.

Regulations stipulate that CMS' collection of information requests must: 1) be the least burdensome means necessary to achieve program objectives; 2) not require duplicative information already available to the Agency; and 3) maintain practical utility.[1] We are concerned the proposed ICR does not comply with these regulations. CMS proposes to require manufacturers to provide an extraordinary level of proprietary and non-proprietary data – some of which CMS already maintains as part of other federal programs (e.g., 340B prices; Medicaid best prices) – within an astonishingly short timeframe (30-days). Clearly, the proposed ICR exceeds the scope and statutory requirements of the IRA, requires burdensome and excessive information with little to no practical utility for CMS, and does not avoid duplication of information available to the Agency. Moreover, we question explicitly whether the Agency has the authority to "request" certain information or categories of information as listed in the ICR. Despite the stated need for such information and the careful statutory framing as a "negotiation," GSK offers that there are limits to what manufacturers can produce as part of a "negotiation."

[1] 5 C.F.R. § 1320.5(d)(1)(i)-(iii).

We respectfully submit the additional comments below to address these concerns and to highlight issues of paramount interest to GSK and the patients we serve.

Flexibility with manufacturer submission of required data elements will be necessary – particularly in the early years of the Medicare Drug Price Negotiation Program

Data submission for required data elements, specifically R&D costs and recoupment of R&D costs, will require manufacturers to apply a set of assumptions to available data when determining monetary amounts. Depending on the set of assumptions applied and the range of approaches selected by the manufacturer, the calculated monetary amounts could vary. It is important to note that applying different assumptions that produce different results is not inherently incorrect. Manufacturers have varying definitions of costs (e.g., enterprise costs, costs to market a product) and of the full scope of cost versus cost recovery. For instance, a manufacturer of HIV/AIDS treatments will confront higher costs when launching products in undeveloped countries. Therefore, CMS should allow for flexibility of different approaches that can be utilized by manufacturers to explain assumptions and provide rationales when submitting required data elements.

It is important to recognize that manufacturers are being required to retroactively submit data that may or may not have existed prior to the passage of the IRA. This includes data elements that the IRA could not have been contemplated with regards to data capture or management prior to the IRA. Accordingly, the requested data may no longer exist, may not exist in the requested form, or manufacturers may not have access to data, along with the recordkeeping and document retention capabilities, that would allow them to recall the costs at the level of specificity that CMS is requesting in the ICR. CMS' proposed data elements are burdensome, subject to different methods and interpretation, and do not necessarily capture the most relevant information to inform a "negotiation."

Data collection could be particularly challenging for products with a long history of development or those that were acquired from different entities earlier in their lifecycle and the requested data simply does not exist due to the transfer of an asset, document retention policies, or other legitimate reasons. It is impractical to assume that manufacturers can retroactively comply with new CMS policies, which is why flexibilities are needed to adjust manufacturer practices moving forward.

GSK encourages CMS to limit data elements to those that are required by IRA statute. For example, in the ICR, CMS seeks to collect price reporting metrics through new methodologies including variations of "U.S. commercial average net unit price" and "manufacturer average net unit price to Part D plan sponsors" – both of which are not referred to by IRA statute. CMS should eliminate data points that are not specifically called out in statute, which we understand to be limited to submission of non-FAMP data only. This will help streamline the data submission process for both CMS and manufacturers.

CMS should utilize data sources that are available within other federal health agencies (such as the VA, DOD, FDA, NIH, etc.) to lower the burden of information placed on manufacturers. For example, non-FAMP is already reported by manufacturers to the US Department of Veterans Affairs. CMS can alleviate burden of the data request by allowing manufacturers to authorize CMS to access information available through other sources.

One way CMS could foster flexibility in manufacturer submission is by removing word limits or at a minimum allow a 3,000-word limit for all data fields. Currently, word limits range anywhere between 100 –

3,000 words, which will likely be insufficient to explain manufacturer assumptions, rationales, and approaches used.

In addition, GSK is concerned CMS will not establish the necessary confidentiality and security measures to protect the substantial volume of proprietary data that CMS will collect. We recommend CMS implement measures beyond the protections of Freedom of Information Act (FOIA) Exemption 4 outlined in the initial guidance for the program, release a confidentiality policy for stakeholder comment, and ensure contractors or others with access to the manufacturer data have agreements with CMS to protect release of the proprietary information.

Finally, CMS should provide manufacturers a mechanism to provide feedback on the process of providing requested data elements for the negotiation program. Manufacturers and CMS would benefit significantly by ensuring a robust feedback mechanism is in place to share lessons learned and discuss ways to improve the data collection and submission process. Successful implementation of the negotiations program will require strong partnership between CMS and manufacturers.

The proposed Primary and Secondary Manufacturer framework adds complexities to manufacturer data submission

Under the proposed framework, CMS intends to sign a negotiation agreement with only the Primary Manufacturer and requires the Primary Manufacturer to collect and report necessary information applicable to any Secondary Manufacturer(s).[2] GSK believes the Primary/Secondary Manufacturer framework poses additional complexities for required data submission. Manufacturer information can be collected by different methods and reported using specific assumptions by an entity. Requiring the Primary Manufacturer to collect, report, and certify the accuracy and correctness of the Secondary manufacturers' data is not feasible because the Primary Manufacturer does not have access to other manufacturer data, cannot obligate the Secondary Manufacturer to provide the data, and would have no way to ensure another manufacturer's data are accurate. CMS should require the Primary and the Secondary Manufacturer to submit and to certify their respective data and should modify the terms of the certification by removing the requirement for completeness, unless CMS provides further guidance on the definition of "complete" to include only the information a manufacturer reasonably has in its span of control.

CMS' proposed framework exposes the Primary Manufacturer to potentially significant Civil Monetary Penalties if the data is deemed false. Additionally, the Primary Manufacturer could have other contractual agreements or legal obligations that limit its ability to collect and report required data. For example, a Primary Manufacturer may violate competition laws if it collects pricing information from a Secondary Manufacturer. The added complexities and burden of data collection by the Primary Manufacturer is another reason why the Primary / Secondary Manufacturer framework should be abandoned by CMS in its final Medicare negotiation guidance.

[2] Centers for Medicare & Medicaid Services. "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments." March 15, 2023.

CMS should take a transparent and public approach to selecting therapeutic alternatives

CMS plans to identify pharmaceutical therapeutic alternatives for each indication of a selected drug using manufacturer submitted data, widely accepted clinical guidelines, and peer-reviewed studies. GSK fundamentally discourages this approach because it could impede a healthcare provider's ability to prescribe the best treatment for a patient.

If CMS moves forward with the therapeutic alternative framework, we recommend that CMS carefully consider the totality of evidence when identifying therapeutic alternatives, including clinical trials and pre-/post-approval real-world evidence that inform appropriate comparators. CMS should take a methodologically rigorous, data-driven, and patient-centered approach based on the standard of care and clinical decision-making to reviewing evidence. CMS should strictly avoid any bias that could impact therapeutic alternative selection and MFP determination.

Additionally, GSK urges CMS to publicly identify therapeutic alternatives, as well as any resources it relied upon to identify the therapeutic alternative and communicate this information upon announcement of the drugs selected for negotiation. CMS should also provide a strong justification as to why the identified therapeutic alternatives are appropriate, driven by clinical guidelines and patient need rather than cost.[3]

CMS currently asks respondents to submit all information on all potential comparators across all indications within the 30-day deadline, without bounds on the possible universe of products. GSK is concerned about the unrestricted nature of this question and the practical utility to CMS of such an open and undefined data set. CMS should consider and prioritize high quality, patient-centered, and robust real-world evidence that is provided by clinicians with the necessary expertise, and by manufacturers – who are in a strong and unique position to inform the determination of appropriate therapeutic alternatives for a selected drug based on their extensive expertise and research on the benefits and impacts of their medicines throughout the product lifecycle. GSK encourages CMS to work with manufacturers on selecting therapeutic alternatives and allow manufacturers sufficient time to review any additional research conducted by the Agency, as well as submissions from other stakeholders.

CMS should clarify evidence standards for submitted data

GSK urges CMS to provide additional clarification on the evidence standards for submitted data (such as, guidance on whether studies must be U.S.- based, types of studies accepted, rigor, evidence hierarchy etc.) to ensure CMS receives appropriate information. This will provide much needed guidance to data submitters and allow them to only include Agency-required evidence. Additionally, as CMS collects evidence from multiple stakeholders, the Agency should indicate whether there are levels of evidence that must be met for provided data to ensure submission and evaluation of high-quality and rigorous evidence. CMS should also provide transparency and visibility on how it will conduct its review of the evidence and provide further guidance on how this information will be disclosed to manufacturers and other data submitters.

GSK further questions the range of topics in which CMS is requesting input from the patient advocacy community. Currently, the guidance seems to suggest that advocates and other stakeholders may only

[3] Pharmaceutical Research and Manufacturers of America (PhRMA). "Comment Letter on the Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments." April 14, 2023.

submit information on the topic of therapeutic alternatives. We recommend that CMS provide advocates an opportunity to provide input on the unique qualities of a product as it relates to their experiences and to share qualitative data on the value of a drug to special populations and for unmet needs.

GSK appreciates the opportunity to provide comments on the Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act. We stand ready to engage with CMS on this critical work to ensure the program is implemented without adverse impacts to Medicare beneficiaries. Please do not hesitate to contact me at Harmeet.S.Dhillon@gsk.com, should you have any questions or requests for additional information.

Respectfully,

Harmeet Dhillon
Head, Public Policy
GSK

VIA ELECTRONIC SUBMISSION

May 22, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: **RE: Information Collection Request (ICR) for Negotiation Data Elements (CMS-10847)**

Dear Administrator Brooks-LaSure:

Haystack Project appreciates the opportunity to provide comments on the Centers for Medicare & Medicaid Services' (CMS') Information Collection Request for Negotiation Data Elements (the ICR).

Haystack Project is a 501(c)(3) non-profit organization enabling our membership of 140+ rare and ultra-rare disease patient advocacy organizations to coordinate and focus efforts that highlight and address systemic reimbursement obstacles to patient access. Our core mission is to evolve health care payment and delivery systems with an eye toward spurring innovation and quality in care toward effective, accessible treatment options for all Americans. We strive to amplify the patient and caregiver voice in these disease states where unmet need is high and treatment delays and inadequacies can be catastrophic.

Patients with rare and ultra-rare conditions rely on health system and public policy priorities that give investors a level of comfort that the costs of research and development can be recouped, either through the price of the new drug, its use in other patient populations, or both. Without this, there is little reason for Haystack Project's patient and caregiver communities to hope that resources will be invested in advancing the treatments we need. Our comments (attached) to CMS' Initial Guidance implementing the Drug Price Negotiation Program under the Inflation Reduction Act (IRA) articulate our concern that the negotiation processes will fail to consider treatment value for rare patients and ultimately negate the incentives that have enabled development of new treatments and maintained commercial viability of existing therapies.

Haystack Project is concerned that the sufficiency of the data elements within the ICR and the burden associated with providing that information are inextricably linked to and vastly

impacted by the Initial Guidance. Haystack Project remains concerned that the most impactful policies and interpretations within the Initial Guidance were finalized without opportunity for public notice and comment and create a drug price negotiation program that has a greater potential to disrupt access to current and future treatments than the plain language of the IRA likely contemplates much less requires. Moreover, the Initial Guidance policies increase the ICR's burden on manufacturers and decrease the extent to which the information collected aligns with the IRA's apparent goal of ensuring that Medicare drug prices reflect treatment value without disrupting incentives toward innovation, including longstanding statutory incentive frameworks that have driven innovation in rare disease therapies.

The ICR represents a procedural and substantive guardrail to ensure that public comment is fully considered. This guardrail is important when the information collection is based on underlying policy determinations and interpretative rules rather than the plain meaning of the statute; it is crucial when those policies and rules were not subjected to public notice and comment.

Our comments emphasize the need for CMS to:

- Reconsider use of moiety or active ingredient rather than NDA/BLA to identify negotiation-eligible drugs because is particularly harmful for securing approvals for small population conditions, further building on IRA provisions harmful to rare and especially ultra rare diseases

- Revise its Primary/Secondary Manufacturer framework so as not to inappropriately over burden rare disease manufacturers and other entities that either license their developed products or acquire and commercialize new treatments

- Re-work the process for non-manufacturer submissions on alternative therapeutic options which, as proposed, is so onerous and limited that it appears designed to discourage patient, advocacy organization and clinician input.

CMS' decision to identify negotiation-eligible drugs based on moiety or active ingredient rather than NDA/BLA overburdens manufacturers and dilutes the nexus between a "monopolist" drug and its value to patients.

Haystack Project had anticipated that CMS would identify negotiation-eligible drugs on the basis of NDA/BLA approvals given the statutory reference to NDA/BLA approval date in identifying negotiation-eligible drugs. CMS' decision to broadly define qualifying single source drug' for negotiation eligibility purposes was unexpected and will likely negate existing incentives for securing approvals in small population conditions and place burdens on industry stakeholders that were not likely contemplated when the statute was enacted.

- Under CMS' definition, a drug with an NDA/BLA approval could be negotiation-eligible earlier than the 9 or 13 years outlined in the IRA if a reference drug is negotiation-eligible. In fact, drugs, including orphan drugs with statutory exclusivity, approved after selection and negotiation would be subject to the maximum fair price.

    - This is not a simple implementation of a statutory requirement; it appears to be an Agency policy determination driving a statutory interpretation beyond and in likely conflict with the plain language of the IRA.

    - Haystack Project members have brought us anecdotal reports of manufacturers shutting down research and development efforts toward new indications for existing drugs and re-focusing efforts away from ultra-rare to more robust orphan indications due to perceived inability to recoup research costs on a drug subject to an MFP at or shortly after approval.

    - Unless CMS retracts its determination to include all NDAs/BLAs for a product as a singular qualifying single source drug for negotiation purposes, our patients have little hope that manufacturers will be able to justify to their shareholders that investing in NDA/BLA approvals for ultra-rare uses of existing treatments is a sound business decision.

- CMS' definition of qualifying single source drug will place information collection burdens on manufacturers that Congress did not consider in drafting the IRA.

    - The scenario examples set forth in the Initial Guidance contemplate requiring the primary manufacturer (NDA/BLA holder) to assume full responsibility and liability for participation in the negotiation process, submission of complete, accurate information and access to the MFP regardless of their role in commercialization activities.

    - Manufacturers often develop drug candidates and then license one or more current or future indications to a commercialization partner. In these instances, research and development costs are split across multiple entities and a manufacturer with data on those costs may not have access to data on sales volume, revenue, and other data elements required within the ICR.

- The MFP is a single price for a drug under the Medicare program. The IRA negotiation process outlines considerations such as alternative therapies, unmet need, and the extent to which a treatment represents an advance in therapeutic options.

    - Had CMS adhered to the NDA/BLA driven approach to drug selection outlined in the IRA, data collected on a drug's value to patients would be clearly related to the NDA/BLA and the patients and conditions to which it applies.

- Aggregating NDAs/BLAs into a single negotiation-eligible drug reduces the nexus between data collected and the true value of the treatment to patients.
    - The value determination will place unwarranted emphasis on large patient populations in disease states with multiple treatment options.
    - Any value in treating rare and ultra-rare patients will be diluted and ultimately rendered irrelevant. This would be the case even if the drug was the only approved option in treating a life-threatening disease.
- Information on alternative therapies is indication-specific. CMS' decision to utilize costs of alternative therapies in calculating an initial offer does not appear reasonable unless the selected drug is defined by an NDA/BLA rather than moiety or active ingredient.
    - Aggregating NDAs/BLAs with multiple, potential diverse, indications and patient populations would lead to a MFP that aligns with the NDA/BLA with the largest patient population.
    - Applying an aggregated alternative-therapies-based initial offer to an NDA/BLA in a small disease population for which alternative treatments are either more costly or nonexistent would, for practical purposes, ignore the considerations the IRA outlines as part of the negotiation process. The negotiated price, as applied to that NDA/BLA would be driven by value, time on the market, research costs, and other factors applicable to a different drug treating a different condition.
        - Haystack Project believes that this result is bad for rare and ultra-rare patients waiting for a treatment to come to market and that the MFP, as applied to that NDA/BLA, would be arbitrary rather than negotiated.

- CMS' definition of unmet medical need is narrow and fails to consider unmet needs associated with patient subpopulations, or a general need within a condition that is not adequately addressed by available therapeutic options.
    - Failure to determine unmet need based on NDA/BLA will make it impossible for CMS to incorporate actual, real-world unmet needs across divergent patient populations and disease states. Once again, aggregating unmet need will yield a result that provides an inaccurate, arbitrary result for indications with multiple, effective therapies as well as those indications for which few options exist.

Haystack Project remains concerned that CMS' Primary/Secondary Manufacturer structures will overburden manufacturers, particularly the small biotech and pharmaceutical manufacturers that have historically developed rare disease treatments.

Arrangements between an early-stage innovator and a larger manufacturer with commercialization expertise are common in the rare and ultra-rare disease space. Agreements between manufacturers are generally based on contracts negotiated and executed well before the parties perform any manufacturing, distribution, and/or marketing activities, and are based on the laws and regulations in place at the time. Neither the IRA, the ICR, nor CMS' Initial Guidance provide for any mechanism through which a primary manufacturer can secure information required within the ICR from a secondary manufacturer.

While CMS might assume that manufacturers can contract with each other to accommodate the IRA requirements, the substantial liability and potential monetary penalties placed on primary manufacturers creates an extremely unlevel playing field. This construct also increases the level of risk associated with investment and partnering opportunities in rare disease treatments initially developed by a pre-clinical manufacturer.

Haystack Project urges CMS to refine its approach given that the burden associated with providing information a manufacturer has no legal recourse to access, much less disclose, is both enormous and avoidable.

The ICR appears to purposefully discourage the public input on alternative therapies and unmet need that it purports to indicate is crucial to the negotiation process.

The ICR provides for public input into the consideration of alternative therapeutic options. Unfortunately, the process for submission, limitation of information content and quantity, and certification requirement will substantially deter patient advocacy organization input.

- The 30-day comment period is far too short for organizations like Haystack Project to collect specific, meaningful input from our member organizations and incorporate the feedback into a comprehensive comment.

- Most patients with rare and ultra-rare conditions have no FDA-approved treatment options and rely on off-label uses of existing treatments. These uses are rarely included within the compendia CMS lists as acceptable sources of information on off-label indications.

    - CMS should ensure that rare and ultra-rare disease patients can provide information on their off-label treatments, potential alternatives, unmet need, and the extent to which their prescribed therapy has improved their quality of life, slowed disease progression, or otherwise improved outcomes.

- CMS has not articulated how the information and scientific evidence it collects will be used to inform decisions on therapeutic alternatives or what evidence is particularly important in the negotiation process.

- Rare and ultra-rare disease patients will find it difficult to challenge CMS identification of an alternative treatment option unless CMS provides information on the treatments it is considering. For example, CMS may focus on a high-volume indication and identify multiple treatment options that could be substituted for the selected drug.

    - Our patient communities cannot provide information on whether or not those therapies are, in fact, actual options in treating their condition or contraindicated/ineffective unless we know what those alternatives are.

    - Without that information, patient advocacy organizations may be able to identify condition-specific options or state that there are no alternative therapies. The ICR and CMS' Initial Guidance do not provide information on how this relatively nonspecific information would be weighed against data on alternative therapies for more common conditions.

- Haystack Project expects that CMS' decision to use the HPMS system for ALL information collection activities associated with the drug price negotiation program will make it difficult for patient advocacy organizations to weigh-in throughout the process.

    - How will CMS notify the public that a comment period is available? Patients and patient advocacy organizations do not have current access to HPMS. We urge CMS to use the notice and comment processes established within regulations.gov to provide notice and receive comments from the public.

- Limitations on the number of words or citations that can be submitted to CMS are unlikely to improve the quality or relevance of information received. We urge CMS to remove those limitations and to encourage stakeholder input relevant to the drug price negotiation.

- The ICR's Section J, *Certification of Submission for Respondents Who Are Not Primary Manufacturers Required for All Respondents Who Are Not Primary Manufacturers***,** is an onerous requirement that implies potential civil or criminal liability. It is inappropriate and unnecessary when applied to patients, patient advocacy organizations and clinicians.

    - Patients and their advocacy organizations must certify that the information is complete and accurate, yet CMS does not provide any guidance on what would constitute a complete submission from patient stakeholders.

- Non-manufacturer stakeholders must also certify that they will "timely notify CMS if I become aware that any of the information submitted in this form has changed." A potential commenter may infer an obligation to inform CMS about changes in medication or symptoms, appearance or reduction of side effects, changes in out-of-pocket costs, emergency room visits, and other health care encounters.

    - There does not appear to be a simple, identified process through which non-manufacturer stakeholders would submit updated information.

- Finally, patients and patient advocacy organizations must acknowledge that they "also understand that any misrepresentations may also give rise to liability, including under the False Claims Act."

    - Haystack Project expects that this provision will significantly deter stakeholders from providing CMS with information that would improve the negotiation process and the data upon which the Agency will rely.

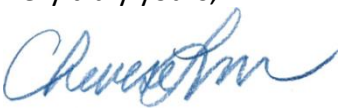
    - If CMS expects that this certification requirement is a necessary part of its information collection, it should narrow the set of stakeholders to which it would apply.

Conclusion

Haystack Project appreciates the opportunity to submit feedback on the ICR, and view this process as critical to ensuring that CMS implementation of the drug price negotiation program is consistent with the language and intent of the IRA. Our member organizations have significant concerns that the decisions CMS makes within the next several months will determine the set of new treatment options in rare and ultra-rare conditions and rare cancers for the foreseeable future. More importantly, the decisions likely to have the greatest impact have been made without public notice and comment or a meaningful dialogue between CMS and the rare and ultra-rare disease community.

Once again, we thank you for your consideration of our comments. If you have any questions, please contact our policy consultant M Kay Scanlan, JD at 410.504.2324.

Very truly yours,



Chevese Turner
CEO
Haystack Project
chevese.turner@haystackproject.org

May 18, 2023

Dr. Meena Seshamani, M.D., Ph.D.

Director, Center for Medicare

Centers for Medicare and Medicaid Services

Department of Health and Human Services

RE: The Negotiation Data Elements ICR Form for manufacturer-submitted data elements and evidence about alternative treatments

Dear Dr. Meena Seshamani, M.D., Ph.D.,

Thank you for the opportunity to comment on the negotiation data elements for manufacturer submitted data and evidence about alternative treatments to support implementation of sections 11001 and 11002 of the Inflation Reduction Act (IRA) (P.L. 117-169), which establishes the Medicare Drug Price Negotiation Program to negotiate maximum fair prices for certain high expenditure, single source drugs and biological products.

My comments on the negotiation data elements are reflective of my experiences as a Health Economist in the pharmaceutical industry generating and leveraging evidence for Health Technology Assessments and drug price negotiations with government payers, primarily outside of the United States. I am also a Doctoral student in Health Policy at Johns Hopkins Bloomberg School of Public Health. The comments I have provided below are my own and do not reflect the opinions of any organizations that I am affiliated with other than myself.

In the final version of the Negotiation Data Elements ICR form it is critical that CMS provide more specificity regarding the information that should be generated and provided to assess a drug's therapeutic impact and comparative effectiveness in Question 41.

My first comment on Question 41 is referring to the instructions. It currently states, “Specify the therapeutic alternative and indication of the selected drug that you are discussing”. This statement requires clarification regarding how the appropriate “therapeutic alternative” will be determined. Dr. Ziouani, Dr. Granados and Dr. Borget assessed the most common approaches to determining therapeutic alternatives for comparative effectiveness assessments in their publication, “How To Select The Best Comparator? An International Economic Evaluation Guidelines Comparison”. It was determined that the most common approach to selecting a therapeutic alternative is to use the standard of care for local practice. Standard of care can be determined by referencing treatment guidelines and should be pre-specified by CMS for each selected drug.

My second comment on Question 41 is also referring to the instructions. It currently states, “When discussing the therapeutic impact of the selected drug, indicate outcome(s) used, the indication(s) to which the evidence applies, and the therapeutic alternative(s) to which the evidence applies.” This statement is ambiguous as currently written and requires more clarity on the outcomes of interest. Potential outcomes of interest could be the primary and secondary endpoints that were included in the clinical trial which was used to achieve FDA approval.

My third comment on Question 41 is referring to the question, “To what extent does the selected drug represent a therapeutic advance as compared to existing therapeutic alternatives? Please discuss for each indication of the selected drug, as applicable.” The definition of a “therapeutic advance” must be explicitly stated. A drug can be considered a “therapeutic advance” for a variety of reasons, which may differ by therapy area. Common attributes associated with “therapeutic advances" include improvements in clinical endpoints, improvements in a patient's quality of life and ability to do daily activities, and a reduction in adverse events associated with currently available therapies.

Dr. Aris Angelis and Dr. Panos Kanavos have identified several attributes generally taken into consideration by payers, clinicians and patients when assessing the value of a medicine in their publication, “Multiple Criteria Decision Analysis (MCDA) for evaluating new medicines in Health Technology Assessment and beyond: The Advance Value Framework.” The attributes highlighted include burden of disease (severity, prevalence, availability of treatments), therapeutic impact (clinical endpoints and quality of life), safety (adverse events, tolerability and contraindications), innovation (nature of treatment and ease of use), and societal impact (improving public health, improving productivity, reducing other healthcare costs).

Some of these attributes may not be appropriate for the Medicare Drug Price Negotiation Program given the program will be focusing on single source drugs that have been approved for at least 7 years or biological products that have been approved for at least 11 years. Additionally a societal perspective may not be appropriate for Medicare given the intention of the Drug Price Negotiation Program is to lower the price of some of the costliest single-source brand-name Medicare Part B and Part D drugs. Therefore, the attributes that CMS should consider when defining a “therapeutic advance” should at minimum include burden of disease, therapeutic impact and safety.

In conclusion, Question 41 of the final Negotiation Data Elements ICR form should include the following clarifications:

- The existing therapeutic alternative should be the standard of care for the disease of interest. Standard of care can be determined by referencing treatment guidelines and should be pre-specified by CMS for each selected drug.
- The outcomes of interest should be the primary and secondary endpoints that were included in the clinical trial that was used to achieve FDA approval.
- A therapeutic advance should be defined as a reduction in burden of disease, a significant improvement in clinical endpoints or an improved safety profile compared to standard of care.

Thank you again for the opportunity to comment on the negotiation data elements for manufacturer submitted data and evidence about alternative treatments for the implementation of the Medicare Drug Price Negotiation Program. If there are any questions regarding my recommendations please do not hesitate to contact me via email at dnbargo@gmail.com.

Sincerely,

Danielle Bargo

May 22, 2023

VIA Electronic Filing – *IRARebateandNegotiation@cms.hhs.gov*

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

RE: Information Collection Request (ICR) Form for Negotiation Data Elements Under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB0938-NEW)

Dear Administrator, Seshamani:

On behalf of Johnson & Johnson (J&J) we submit the following comments in response to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Information Collection Request (ICR) Form for Negotiation Data Elements Under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB0938-NEW).*[1] J&J is the world's most comprehensive and broadly-based manufacturer of healthcare products for pharmaceutical, medical devices, and diagnostics markets. For nearly 130 years, we have led the way in innovation and are continuing this heritage today by bringing important new pharmaceutical products to market in a range of therapeutic areas on behalf of all our current and future patients, including Medicare, Medicaid, and Marketplace beneficiaries.

We are engaged members of BIO and PhRMA and endorse their comments also submitted in response to this ICR while providing further input below. On April 14, 2023, J&J submitted our significant feedback related to the negotiation factors in comments filed in response to the *Medicare Drug Price Negotiation Program (Program or the Program): Initial memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance, the Guidance). The comments provided in response to this ICR are aligned with our feedback submitted in response to the Guidance. We encourage CMS to consider both of our responses in their entirety and in conjunction with one another.

J&J appreciates the collaboration with CMS in the implementation of the IRA. In recent public forums, Medicare leadership has laid out an implementation framework grounded in the principles that the Program administration must be pragmatic and operationally feasible and that the negation component will place the true value of the drug, in particular the value a selected drug delivers to the Medicare population, as the focal point of the negotiation. J&J is aligned to this implementation framework.

Inexplicably, however, the proposed ICR is entirely at odds with the above framework. First, this ICR requires a significant volume of information that is in excess of the statutory requirements needed for the factor analysis. Second, the data evidence requirements are not focused on the evidence required to assess a drug's value over time for the Medicare population; instead, volumes of data are requested on the cost

[1] Available at https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847

factors Third, this ICR imposes substantial requirements, with mandated certification under significant penalty, for collection of data that is not operationally feasible within current business, financial and operational practices, and systems.

We offer three principles to guide a substantially revised version of the ICR:

1. Align reporting requirements directly with, and not exceeding, the statute;

2. Prioritize operational feasibility and simplicity, including leveraging data already required for federal reporting programs, utilizing information and resources otherwise available within the Government, and delaying requests for information that are not critical for year-one operations; and

3. Commit to prioritizing those factors that emphasize value to the Medicare beneficiary. This flexibility is offered in the statute.

Across the industry, considerable modifications and changes to internal systems would be necessary to meet the requirements outlined in this ICR. It is highly improbable that manufacturers would be able to meet these requirements, generating burden for CMS, and statements of non-compliance for impacted manufacturers. As a solution and more feasible approach, we encourage CMS to establish the MFP at the ceiling price in the initial years of the Program. Such an approach offers all parties to the negotiation more predictability and stability in the early years of Program implementation with the added benefit of more time and thoughtful analysis regarding needed data submissions.

As the Agency works to implement the many statutorily required components of the Program, and in particular, the analysis of manufacturer-specific data and evidence on treatment alternatives, we urge CMS to consider the significant influence these policies will have on the innovation ecosystem. Specifically, our collective efforts to put world-class healthcare consistently within reach of our beneficiaries and patients and to continuously improve medicines depend upon how high-value services are defined and incentivized. Contextual value drivers of health and healthcare must be emphasized and considered within the data analysis, for example, the value of real-world evidence in establishing context on therapeutic alternatives, equitable access, and the considerable formulary implications impacted by this Program.

Given our significant concerns and interest in the Program, we urge CMS to consider our priority recommendations below and the following comments on specific sections of the ICR.

Prioritized J&J Recommendations in Response to the ICR:

- Establish MFP at the ceiling price in the initial years of the Program to promote operational feasibility and limit reporting burden;

- Directly align reporting requirements to those required under statute, removing requirements for any additional information;

- Prioritize evidence of therapeutic alternatives;

- Remove mandatory reporting of pricing data other than non-FAMP that are not required by statute or relevant to the negotiation of the MFP;
- Remove primary manufacturer data submission obligations related to unaffiliated secondary manufacturers;
- Provide flexibility in reporting detail and format with the opportunity for manufacturers to explain information and values reported (applies to all sections of the ICR);
- Adopt the use of the Veterans Health Care Act of 1992 (VHCA) for reporting the nonfederal average manufacturer price (non-FAMP or NFAMP);
- Simplify the R&D reporting requirements to allow manufacturers to offer an attestation when R&D costs have been recouped;
- Remove the requirement to submit information on R&D tax credits, which are not addressed in statute and are not product-specific;
- Clarify that expired and non-public patents are not required for submission;
- Provide clarity on the process for evaluating evidence about alternative treatments generated through CMS' analysis; and
- Revise the Certification Statement to limit liability and remove requirements of completeness.

J&J Comments on ICR Sections:

GENERAL INSTRUCTIONS

CMS notes that Primary Manufacturers will submit information for Sections A through I via the Health Plan Management System (HPMS). However, the HPMS system currently only allows for one individual per manufacturer to access the system. Because of the significant volume and scope of data required in this ICR, it will be very challenging for one individual to be responsible for the submission. Therefore, for manufacturers to submit data using the HPMS system, CMS will need to update access to the system to allow more than one individual from a manufacturer to access and submit.

Additionally, we reiterate comments previously made concerning the Guidance related to the concept of "primary" and "secondary" manufacturers, where the primary manufacturer will be accountable for the submission of data and pricing actions of unaffiliated secondary manufacturers. We reiterate our concerns with this approach as primary manufacturers do not have access to the required data elements for secondary manufacturers and do not have the needed control or authority to ensure their compliance.

INSTRUCTIONS FOR REPORTING MONETARY AMOUNTS

J&J is concerned with the form, format, and detail of the information requested by CMS, within this section and throughout the ICR. CMS states that when calculating and reporting monetary values, the

information should be consistent with the manufacturer's accounting policies and industry standards[2]. However, the formats outlined in this ICR directly conflict with our existing accounting policies and industry standards, and they would present significant operational challenges for manufacturers. For example, CMS is requesting the submission of monetary data in Section G of this ICR by calendar quarter, but this does not align with our accounting practices which use fiscal quarters. CMS is also mandating reporting of non-FAMP *units* in Section B, which is not data we collect, retain, or currently report, as manufacturers report final non-FAMP, not units, which are a component of the complete calculation. Throughout the ICR, to reduce reporting burdens and the resulting operational complexities for manufacturers, CMS must limit the data required for submission to the data outlined in statute and provide flexibility in reporting detail and format with the opportunity for manufacturers to explain values reported without the restriction of word counts.

SECTION A. SELECTED DRUG INFORMATION

This section calls for manufacturers of selected drugs to submit all 11-digit National Drug Codes (NDC-11) for a selected drug. However, at a foundational level, we are concerned that this reinforces the flawed definition of a qualified single-source drug (SSD) that CMS issued as final in the draft negotiation guidance, which J&J strongly opposes. We reiterate our past comments that CMS' definition of an SSD as finalized in the Guidance represents a significant departure from the well-established statutory definitions and would present significant unintended consequences for Medicare beneficiaries and innovation.

SECTION B. NON-FAMP DATA COLLECTION

J&J urges CMS to adopt the VHCA fiscal year instead of the calendar year for reporting non-FAMP data. Adopting the existing annual non-FAMP calculation based on the four quarters of a federal fiscal calendar year under the VHCA will minimize operational disruptions that may arise with the creation of a new price point based on the calendar year. This is a commonsense opportunity for CMS to leverage data already available within the government, promoting alignment rather than creating a new calculated price point based on the calendar year.

We are further concerned with the requirement to report non-FAMP *units* and the burden this will place on manufacturers. The VHCA does not require manufacturers to submit non-FAMP calculated units. While Non-FAMP units are embedded within the calculation logic, we are not required to and do not store that information in reporting the final non-FAMP. To meet this new reporting requirement, we would have to manually extract and verify the units by calendar quarter for the past five years. We question whether CMS intends to impose this level of burden on manufacturers. We ask CMS to revise this section to align with non-FAMP calculated under the VHCA. Moreover, as manufacturers already report this data under the VHCA, we ask CMS to leverage that data already submitted by manufacturers and not impose an additional reporting burden on them or calculation burden on the Agency.

J&J also recommends that CMS clarify the submission requirements for drugs where there is no non-FAMP data in 2021. For this scenario, CMS states its intent to require the Primary Manufacturer to submit data on the non-FAMP unit type and total unit volume for each NDC-11 of the selected drug for the first full year following market entry for such drug. However, no details are provided to define the

[2] p. 3 Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

phrase "market entry." Therefore, we reiterate our prior comments for CMS to define a market entry in its Final Guidance to provide more clarity around this requirement for manufacturers.

Lastly, as we have stated in past comments, we stress the importance of CMS permitting manufacturers the opportunity to make timely restatements. CMS has not defined a process for non-FAMP restatements or for addressing non-FAMP anomalies which is important for addressing scenarios in which restatements may be necessary or to account for anomalies with reported non-FAMP data.

SECTION C. RESEARCH & DEVELOPMENT COSTS & RECOUPMENT

The Outlined R&D Reporting Requirements Are Operationally Infeasible

In implementing the Program, the IRA requires that the Secretary consider R&D costs and the extent to which manufacturers have recouped these costs. The most straightforward interpretation of the statute suggests that the Agency is charged with considering if a manufacturer, at the time of a drug's selection, has recouped its investment in developing and bringing a therapy to market. The approach that CMS has outlined in the Guidance and again in the ICR goes beyond the intention of the statute and is highly burdensome and unfeasible. While the evaluation of R&D costs and a manufacturer's recoupment of these costs is required by statute, the approach and questions delineated in the ICR are incompatible with existing financial practices, are highly burdensome, and neglect the multi-faceted and interlinked elements that comprise the research ecosystem. We encourage CMS to simplify the R&D reporting requirements outlined in the ICR to allow the Primary Manufacturer to offer an attestation in instances where the manufacturer believes it has fully recouped R&D costs for the selected drug. In instances where the manufacturer indicates that R&D costs have been recouped, then CMS does not need additional information. However, in instances where the manufacturer has not recouped costs, manufacturers should provide more information to the Agency.

In instances where more detailed R&D costs are needed by the Agency, we offer the following considerations to align data submissions more appropriately and realistically with industry practices. Broadly, the sum calculation of all R&D costs is a complex, nuanced, and significant task. For products that will be selected for negotiation for the year 2026, these products will have been on the market for some time and R&D investments will have begun nearly 20 years ago. As such, accurately reporting R&D costs may be particularly challenging and, in certain instances, accurate cost data will not be available.

The Overly Narrow Definition of R&D Costs Does Not Reflect True Costs or Align with Statute

CMS is considering a narrow scope of total R&D expenditures that underestimates the true cost of bringing a new drug to market, which only includes a small subset of drugs that generate significant revenue within Medicare. Considering R&D costs in this way does not accurately reflect the true cost of innovation or the associated risks. CMS' use of such a narrow scope in considering R&D expenditures fails to recognize that manufacturers cannot simply invest in only one product. Negotiation based on this flawed model could have significant adverse effects on companies in the near term and may prove devastating from a long-term perspective as the financial impacts on companies compound over time.

We encourage the Agency to employ great caution in avoiding discrepancies in their calculation for R&D costs and recoupment. For instance, CMS seeks to understand "global lifetime revenue" but only seeks to consider R&D costs associated with "FDA-approved indications." This approach does not align with the

statute, which does not limit R&D to FDA approved indications. Further, it undermines the complexity of drug development which is often conducted on a global scale and to meet the needs of patients all around the world. Limiting R&D investments to those that have only been approved in a US setting while seeking global revenue represents a significant discrepancy in the Agency's approach within Section C of the ICR.

The six categories CMS has proposed to use for the calculation and reporting of R&D costs is a new requirement, distinct from all other submissions with State or Federal agencies or other regular financial filings. In advancing this component of the submission request, CMS assumes that manufacturers have access to this type of information, in the format outlined in the ICR. For example, in Question 1, CMS requests manufacturers to disclose pre-clinical spending for the moiety under negotiation. This question is misaligned with more typical approaches to calculating R&D costs at this stage, which often consider costs across an entire portfolio of therapeutic areas. Instead, CMS should allow increased flexibility in manufacturers' responses to this question to allow for the appropriate cost determination that aligns with internal and/or industry financial practices. Additionally, CMS seeks to consider the cost of abandoned and failed drug costs but utilizes an overly narrow definition of this cost. Industry practice is such that manufacturers calculate total R&D spending more broadly which accounts for the cost of failed drug costs.

Questions:

- In Question 6, CMS solicits additional information from manufacturers on the cost of other R&D for the selected drug not accounted for in questions 1-5. To respond most accurately and completely, we note that this question remains vague and does not clearly define what is acceptable to include in this calculation. As such, we request that CMS clarify the extent of such costs allowed to be included in this question.

- In Question 7, CMS seeks to collect global, total lifetime manufacturer net revenue for the selected drug to determine if the manufacturer has recouped its R&D costs. Aligned with the entirety of information collected in the ICR and our comments in Sections D and G, we strongly encourage CMS to consider the inclusion of other items such as the cost of goods and cost of doing business.

At present, the Guidance and ICR have proposed a highly burdensome and inaccurate approach to calculating R&D costs to determine recoupment which makes it challenging for manufacturers to comply with CMS' data submission requests fully and accurately. To assure manufacturers appropriately comply with CMS' requirements for data submission, we strongly recommend that CMS pursue a single attestation that allows for a more simple, less burdensome approach and more closely aligns with industry practices.

SECTION D. CURRENT UNIT COSTS OF PRODUCTION & DEVELOPMENT

The requirements outlined in the ICR for reporting production and development costs do not promote operational feasibility and would be very challenging for manufacturers. Under this section, CMS outlines the requirements for manufacturers to report the average unit costs of production and distribution for all the NDC-9s included in the selected drug. J&J is concerned that the methodology CMS is prescribing for determining production and distribution costs is not outlined in statute and relies on data that may not be available to manufacturers. We ask CMS to increase flexibility by allowing manufacturers to report a

value and provide an explanation detailing how production and distribution costs were calculated. While aligning with the statute, this approach would also mitigate operational challenges resulting from an overly prescriptive methodology that does not align with a manufacturer's accounting practices or cost-tracking methods.

Additionally, we note that the NDC-9 reporting requirement under this section does not align with the non-FAMP reporting under Section B of this ICR, which uses NCD-11, adding to the excessive data collection and reporting burden for manufacturers.

We also urge CMS to clarify that royalty expenses should be included in the costs of production and distribution. Often, manufacturers license rights to intellectual property or technology and pay royalties as part of those licensing agreements. The royalties are integral to the production and distribution of the drug and therefore should be included in this section.

SECTION E. PRIOR FEDERAL FINANCIAL SUPPORT

While prior federal financial support is outlined in statute, J&J reiterates that CMS should not impose an unnecessary reporting burden on manufacturers to provide data that is already accessible to the Agency within the Government. J&J urges CMS to leverage data available from other sources, such as data directly available through government grant programs that provide financial support to manufacturers. We are also opposed to the overly prescriptive reporting format and, as stated above, to promote operational feasibility, we encourage flexibility in reporting that would permit manufacturers to submit a single federal financial support number along with an explanation detailing the support included.

Further, the CMS requirement to submit information on R&D tax credits exceeds the statutory requirements. We ask that CMS remove this requirement. The US tax credit for R&D is a credit for increasing R&D activity, requiring entities to surpass a baseline level of R&D spend[3]. It is aggregated and cannot be directly correlated between dollars spent and credit received for any single product. For example, for J&J, the R&D credit is based on the consolidated filing of all J&J legal entities included in the filings, which spans beyond pharmaceuticals and includes consumer goods, medical technology, etc. Therefore, these tax credits which are not product-specific and not required by the IRA should not be considered for this section as it is impossible to allocate the credit at a product-specific, or even sector-specific, level.

SECTION F. PATENTS, EXCLUSIVITIES, AND APPROVALS

CMS seeks to collect information regarding the selected drug's relevant pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals by the FDA. We encourage the Agency to clarify that expired patents and non-public patents are not required for submission, but rather should be disclosed at the discretion of the Primary and/or Secondary Manufacturer.

[3] 26 U.S. Code § 41 https://www.irs.gov/pub/irs-regs/research_credit_basic_sec41.pdf

SECTION G. MARKET DATA, REVENUE, AND SALES VOLUME DATA

The requirements outlined in Section G far exceed the description in the statute of manufacturer submission of "market data and revenue and sales volume data". In particular, the Agency's request for product-specific acquisition costs, detailed and proprietary pricing data from other federal and commercial programs, and gross-to-net revenue calculations, spans well beyond the requirements of the statute. We do not believe CMS has the authority to require submission of pricing data aside from non-FAMP, as non-FAMP is the only pricing metric specified in the IRA, and is the only information needed to establish MFP at the ceiling price. J&J does not support mandatory reporting of additional pricing data points which are proprietary and unnecessary for Program implementation. Section G represents an overreach beyond the authority provided to CMS in statute and is not reflective of a good faith negotiation. J&J urges CMS to remove questions in this section requiring the submission of pricing data beyond non-FAMP and limit the required submission of revenue and sales data to the minimum needed to meet statutory requirements and needed for negotiation.

Moreover, we encourage CMS to remove these questions, as many of the data points outlined in this section are already reported to federal agencies and therefore available to CMS from within the Government, and because many of the questions are unclear. For example, the most recent five-year quarterly reporting requirement is unclear, as it is not discernable if CMS is seeking submission of data on the five most recent calendar years (Q1 2018- Q4 2022) or by quarter (Q3 2018 - Q2 2023). We note that manufacturers will have different fiscal calendars for accounting purposes that may not align with calendar quarters and underscore that requiring submission of data by calendar quarter would impose operational complexity for manufacturers that CMS should strive to avoid.

Further, when National Council for Prescription Drug Programs (NCPDP) unit type is required for submission, the ICR is not clear whether the unit price should be provided at the lowest unit of measure or at the package size. J&J asks CMS to clarify that the package size should be used. Prices at the lowest unit of measure are not consistent with the price that is typically reported and published for certain data sets, such as 340B, Federal Supply Schedule and Big Four Price, which are all at package size, and we suggest that CMS adopt package size price where appropriate. CMS should also confirm that manufacturers should exclude returns in the requested volume data sets.

Question-specific comments are provided below:

- Question 17: Primary Manufacturer Acquisition Costs of the Selected Drug: Acquisition costs are not specifically called out in statute as required reporting, and therefore this information should not be required, and if required, we ask CMS to clarify how such data will be used within the negotiation.

  J&J urges CMS to remove this question which is not required by statute and not needed for the negotiation. This question is unclear and would present operational feasibility challenges. For example, CMS is requiring that manufacturers report the total costs of an acquisition of the NDA / BLA(s) for the selected drug including costs of previously approved or future NDA/BLA(s) of other drugs and biological products if the other drugs and biological products were part of the same acquisition. However, acquisition costs often are not specific to the NDA / BLA, and it would not be feasible to attribute those costs to a specific NDA / BLA. For example, acquisitions could be specific to an NDC or could reflect the purchase of an entire company and its portfolio which may include R&D pipelines for products not yet in the market and technologies associated

with how we research, develop, and manufacture future innovations. Further, it is not clear what specific costs should be included for reporting, such as upfront payments and related milestone payments. Therefore, CMS should remove this question.

- Question 19: Wholesale Acquisition Cost Unit Price
  J&J opposes the inclusion of NDC-9 data in the response form for this question, as WAC is published at the NDC-11 level, not at the NDC-9. CMS notes that any deviation from the reported WAC unit price submitted in response to this question and the WAC unit price reported in wholesale price guides or other publications must be explained in Question 20. Submitting WAC at the NDC-9 would lead to unavoidable discrepancies, requiring manufacturers to explain under Question 20 in almost all cases. Therefore, we urge CMS to revise this question to require the reporting at NDC-11 instead of NDC-9 level. Further, manufacturers do not have access and visibility to all third-party publications and cannot be expected to reconcile pricing information with every third-party publication or be held accountable for the accuracy of their publications.

  Moreover, we note that quarterly WAC publicly available in price guides and other publications is reported based on the effective date. WAC changes can occur throughout the quarter, and therefore, CMS should clarify if quarterly WAC should be reflective of the first or last day of the quarter.

- Questions 21: 340B Ceiling Price; 25: Medicaid Best Price
  J&J asks CMS to remove these reporting requirements because, as noted above, this pricing data is not required for the Program, as they are reflected in prices from separate and distinct programs which should have no bearing on the determination of the MFP. The statute does not require the submission of this data.

- Questions 27: Federal Supply Schedule Price; and 29: Big Four Price
  CMS should eliminate these reporting requirements. The statute does not call for the submission of this pricing data, which is not applicable to or needed to support the negotiation of the MFP. Moreover, the requirements are unclear and would create considerable burden on manufacturers and the Agency. For example, in the ICR, CMS states that the total unit volume is the total number of units for each NDC-11 sold to direct federal purchasers. Federal agencies do not typically purchase directly from the manufacturer, as they typically purchase through wholesalers. These questions should be removed.

- Questions 31: Commercial Average Net Unit Price; Question 33: Manufacturer Average Net Unit Price to Part D Sponsors; 35: Quarterly Total U.S. Gross and Net Revenue; and 37: Quarterly Total U.S. Unit Volume
  J&J underscores that these questions represent new and significant reporting requirements not already calculated or reported by manufacturers for any other program at this level. These data points are not contemplated as information for submission in the statute and would impose a significant organizational burden on manufacturers, as they do not align with existing reporting requirements or accounting procedures. For example, J&J does not calculate or disclose many of the data elements outlined under these questions including Commercial and Medicare Part D average unit net price, average net unit price without patient assistance programs, and best average net unit price; and we also do not calculate gross to net revenue deductions at the NDC

level, as these calculations are done across an entire brand. Moreover, these reporting requirements would create operational challenges in that the NDC-9 reporting does not align with other programs that are at the NDC-11, and the five-year timeframe would be especially onerous for compliance. It would be extremely burdensome to calculate and report such data, and it would not be feasible to do so in the 30 days contemplated in the draft guidance and this ICR. For these questions, we strongly urge CMS to retract the reporting requirements, which are not necessary for the operation of the Program.

Further, we note that the data contemplated in question 33 are not available to manufacturers. CMS is requesting Medicare Part D unit volume; however, J&J would only have visibility to contracted sales unit volume, not total unit volume, and therefore would be unable to validate such data for submission.

SECTION H. EVIDENCE ABOUT ALTERNATIVE TREATMENTS

J&J remains deeply concerned and opposes the approach employed to determine the selected drug's MFP, which, despite CMS' stated intent to use patient value as the starting point for negotiation, overemphasizes manufacturer-specific and cost-related data and undervalues and discredits the importance of a drug's clinical benefit as compared to its therapeutic alternative. As currently proposed, the approach is at odds with determining a drug's unique value based on its impact on patient's health and lives. This is evidenced by the overemphasis on what the Agency considers the mandatory submission of manufacturer-specific data, which is approximately 90 percent of the entire set of questions, compared to what the Agency set as optional submission to questions on the evidence focused on therapeutic impact and comparative effectiveness, unmet need and prescribing. Additionally, the ICR envisions no formal interaction and engagement on these critical value factors prior to CMS offering its determination of the MFP. Neglecting to do so is truly regrettable as manufacturers of selected products are in a unique position to contribute substantial information and perspective in treating a disease and serving a particular population of patients.

We strongly believe there is value for manufacturers and CMS to engage in dialogue earlier in the process on clinical comparative effectiveness, therapeutic alternatives, and therapeutic impact. Take for example, the process employed by Advisory Committee on Immunization Practices (ACIP), in which the manufacturer engages with ACIP in a transparent process with robust dialogue and defined parameters (such as the Evidence to Recommendation Framework) when making recommendations on new or existing vaccines. Similarly, the Food and Drug Administration (FDA) engages with drug developers throughout the process of submission to determine safety and efficacy. We urge CMS to provide the manufacturer the ability to present information on therapeutic comparators to CMS at multiple points during the negotiation process – particularly important prior to CMS' initial MFP determination until the final price is set. Similarly, CMS should also outline its approach for a genuine exchange that defines the parameters of its comparative value assessment. Instituting a more inclusive and transparent process would help CMS to fully understand the evidence landscape and receive feedback on the vital step of the selection of comparator therapies.

In response to the questions outlined within this section of the ICR, CMS specifies word counts, limits the number of citations, and allows text-only responses. We are deeply concerned that the overly restrictive nature and allowable formatting (text only) impose arbitrary limitations on the presentation of relevant information of value and clinical benefit factors. Experience throughout the scientific and medical communities has demonstrated that tables and figures (including charts and graphs) are essential to

represent complex scientific information succinctly. We strongly encourage CMS to allow for tabular and visual representations and remove the word restriction for the manufacturers of negotiated products, who can offer the greatest visibility into the medical literature around therapies they developed. We are also worried that limiting citations does not allow for a holistic representation of the selected drug's value. Medical treatments that have been on the market for many years across multiple indications can easily have hundreds of studies and clinical references explaining the drug's characteristics, value, and patient impact, which should be germane to CMS decision-making. As such, we recommend CMS removes these unnecessary and arbitrary restrictions.

We encourage CMS to revise the Form for Negotiation Data Elements to clarify terminology such as how evidence received and generated through the Agency's own analysis will be appraised. To allow manufacturers the ability to share information accurately, CMS should clarify what precisely is meant by "therapeutic advance and impact" and describe explicitly how this definition is inclusive of diverse patient perspectives and groups. Having sufficient clarity on the process with clear guidance and parameters will enable the manufacturer to develop a robust and tailored submission. To ensure the appropriateness of the data considered, we also urge CMS to provide more guidance on the evidence standards it will apply to received information as well as its internal analyses. Clarity on this point will be particularly relevant for analyses based on real-world evidence as they require discussion on robust methodologies to avoid data misinterpretation that may result from observed and potentially unobserved variables. For example, differences observed in observational research outcomes between therapies may be driven by underlying differences in care, administration, and drug use within the healthcare system and need to be separated from differences in the effectiveness of analyzed therapies. While standard approaches have been proposed to address the matching of real-world populations within and across studies to control for underlying differences, any one model can have limitations that may increase imbalance, inefficiency, model dependence, and bias.[4] We encourage CMS to apply clear requirements of detail and transparency on all model assumptions embedded in the analysis and data generation.

As outlined in our comment response to the Guidance, we encourage the Agency to employ a methodologically sound, transparent, replicable, qualitative, and tailored approach to appraise the value of negotiated therapies to beneficiaries through pertinent data, including real-world evidence and observational research. CMS should completely avoid formulaic assessment methods that rely on generic, potentially discriminatory measures and/ or arbitrary payment thresholds – these include quality-adjusted life years (QALY), the equal value of life years-gained (evLYG), health years in total (HYT), or generalized risk-adjusted cost-effectiveness (GRA)-QALY/ GRACE).

We offer the following additional comments related to the specific questions:

- In question 40, CMS requests information on comparator product labels. It is important to note that in reviewing submissions, CMS should consider that product label comparisons can include studies with different inclusion and exclusion criteria or differing outcomes definitions. Submissions attaching labels without proper context can lead to errors in comparison of products, a practice that is inconsistent with FDA regulations, except for well-controlled, randomized head-to-head studies.

- In questions 41-43, CMS asks submitters to identify the potentially discriminatory impact of submitted evidence in a life extension context. This again raises the question of how CMS intends

[4] https://www.journals.uchicago.edu/doi/full/10.1086/711393

to meet the Agency's statutory obligation not to rely on the QALY or similar metrics. We reiterate our position that the potential for discrimination inherent to the QALY, and its adaptations, is not merely contingent upon the differences in expected longevity. For this and other additional methodological deficiencies in using such metrics, we strongly encourage the Agency to reject the submission of any evidence using the QALY and similar measures categorically and explicitly. In line with FDA Guidance[5], CMS should assess treatments based on disease-specific and patient-centric quality-of-life metrics that holistically capture the value of therapies to their intended populations.

- In question 41, CMS asks for the submission of "current costs" of comparator therapies. Stakeholders involved in the pharmaceutical supply chain can only represent their side of any transaction. Stakeholders without access to direct and proprietary cost information may provide unreliable estimates. CMS should be wary of price and cost "estimates" found in the literature (e.g., net price approximations) that may be inaccurate and contain bias. In addition, the definition of cost to Medicare is unclear. CMS should therefore clarify which 'costs' it refers to in this section. In principle, we believe CMS has access to internal data on drug costs to Medicare which are more reliable than any third-party estimations and should therefore be utilized for cost calculations.

- In question 43, we welcome CMS' attention to special populations and comparative effectiveness, which can represent one form of variability in treatment effect that could have a bearing on health disparities. In addition to patient-level characteristics, CMS should also account for other important sources of heterogeneity (e.g., arising from factors such as socioeconomic differences, geographic variability in treatment patterns and access to care, insurance coverage, as well as variability in patient preferences). We thus reiterate that the Agency should consider the unmet need that may arise from diverse real-world sources. A holistic understanding of these drivers is necessary to comprehensively recognize the therapeutic value.

SECTIONS I & J. CERTIFICATIONS OF SUBMISSION

CMS outlines its intent to require manufacturers to provide certification that information submission is "complete and accurate." We are especially concerned that given the strict word limits outlined in this ICR, it would not always be possible for manufacturers to submit complete explanations or other complete details. We ask CMS to remove "complete" from the certification statement given the limitations imposed by CMS that may inhibit the ability to provide fully complete information for some of the sections. Furthermore, while we agree that the information submitted should be accurate, we reiterate and ask CMS to acknowledge that manufacturers will have made reasonable assumptions given CMS' vague requirements and the significant challenges stemming from conflicts between the requirements outlined in ICR and manufacturer and industry accounting practices. Furthermore, we ask CMS to remove the requirement of timely notification of changed information.

[5] Food and Drug Administration. Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Guidance for Industry. December 2009. https://www.fda.gov/regulatory-information/search-fda-guidancedocuments/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims

The terms of the certification stipulate that any misrepresentation may give rise to liability including under the False Claims Act. Such a liability statement is not required by statute and is not included in similar certifications, such as the Average Sales Price (ASP) certification. We suggest CMS adopt a certification statement like the ASP certification, which requires the agreement that submitted information was done so according to the submitter's best "knowledge and belief" and "made in good faith."

Conclusion

We are very concerned that the ICR as proposed contradictory with the Agency's purported goals of promoting feasibility in implementation and prioritizing patient value in negotiation. The requirements outlined in this ICR far surpass the manufacturer reporting requirements outlined in statute. The creation of new metrics and submission requirements for data not ordinarily collected or maintained by manufacturers in their existing business practices will result in noncompliance issues due to operational infeasibility and considerable operational burdens that are woefully underestimated by CMS. Compounding these concerns, the prescriptive reporting format and restrictive word counts limit the ability of manufacturers to explain submissions and demonstrate value. Building on our comments responding to the Guidance on the Program, J&J is concerned that the reporting requirements outlined in this ICR point to a cost-plus approach to determining the MFP, which does not sufficiently consider value to beneficiaries and the broader impact the MFP may have across all payers.

Congress did not intend for the IRA to create the new reporting metrics and requirements on manufacturers, and associated burden for the Agency, that CMS has outlined in the ICR. Especially in the early years of the Program, it is critical that CMS's framework for implementation and requirements embody simplicity and operational feasibility. We reiterate our recommendation to establish the MFP at the ceiling price in the initial years of the Program, limit data reporting requirements to what is needed to calculate the ceiling price and provide stakeholders with a reasonable opportunity to provide meaningful input on the factors over a more appropriate timeframe.

We are committed to engaging with CMS to implement a Program that prioritizes operational feasibility, and most importantly recognizes the value to beneficiaries as a foundational aspect of determining the MFP. We welcome questions and the opportunity to work more closely with the Agency on the ongoing IRA implementation.

Sincerely,

Jacqueline Roche

Jacqueline Roche, DrPH
Head Payment and Delivery & Global Policy Institute
Johnson & Johnson Worldwide Government Affairs & Policy

MassBio
MASSACHUSETTS BIOTECHNOLOGY COUNCIL

main: 617 • 674 • 5100 fax: 617 • 674 • 5101

Massachusetts Biotechnology Council
700 Technology Square, 5th Floor
Cambridge, MA 02139

May 22, 2023

William N. Parham, III, Director
Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
Centers for Medicare & Medicaid Services
7500 Security Boulevard Baltimore, Maryland 21244

RE: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

Dear Mr. Parham:

The Massachusetts Biotechnology Council (MassBio) appreciates the opportunity to submit comments on the Centers for Medicare & Medicaid Services (CMS) proposed information collection request (ICR) for the Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA).[1]

MassBio represents the premier global life sciences and healthcare hub of Massachusetts, which has a vibrant biomedical research and development community that is a global leader for medical discovery and innovation. MassBio's 1,600+ member organizations are dedicated to preventing, treating, and curing diseases through transformative science and technology that brings value and hope to patients. MassBio's mission is to advance Massachusetts' leadership in the life sciences to grow the industry, add value to the healthcare system, and improve patient lives.

As described in our recent comments in response to CMS's initial guidance regarding the Medicare Drug Pricing Negotiation Program ("Negotiation Program"), MassBio is deeply concerned about the impact the Negotiation Program will have on the future development of innovative and life-saving therapies, as well as on the world-leading small and emerging biotech companies based in Massachusetts. Given the potential impact on innovation and thus on vulnerable patient access to life-saving therapies, we continue to urge CMS to adopt a "do no harm" approach in implementing this program that errs on the side of mitigating against the potential disincentives created by the program's framework, and that allows the agency to make corrections as needed to preserve innovation. To these ends, it is essential that the information CMS collects for purposes of the Negotiation Program fully captures the value of a given selected drug.

The IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider certain "manufacturer-specific data," which includes, among other things, research and development (R&D) costs. As outlined in greater detail, below, MassBio urges CMS to broaden the definition of R&D costs to enable CMS to accurately assess the true scope of these costs in the innovation ecosystem.

The IRA also directs CMS to consider "evidence about therapeutic alternatives." This includes the extent to which the selected drug represents a therapeutic advance and the extent to which the selected drug and its therapeutic alternatives address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy. In the ICR Form, CMS provides only the most general

[1] 88 Fed. Reg. 16,983 (March 21, 2023).

of questions regarding each of these dimensions, which is unlikely to generate the type of information CMS needs to consider the therapeutic impact of a given selected drug, let alone compare that drug to any therapeutic alternatives. To improve the quality, utility, and clarity of the information to be collected, MassBio recommends that CMS:

- Make the process less burdensome for the public to submit information regarding the negotiation factors in section 1194(e)(2) of the Social Security Act;
- Solicit information regarding key pharmacological dimensions and patient-centered impact to better compare selected drugs to their therapeutic alternatives;
- Solicit information on the impact on rare disease and mental health in assessing the impact of a selected drug on specific populations, and take additional steps to ensure that quality-adjusted life year (QALY) data are excluded from consideration; and
- Broaden the definition of unmet need, with a lens specific to health equity, and consider whether a selected drug addresses an unmet need on an indication-specific basis.

I. To improve the quality and utility of the information collected for the Negotiation Program, CMS should redefine the R&D cost questions to better reflect the complexity of the innovation ecosystem.

As outlined in the ICR Form, CMS is collecting information regarding a combination of costs incurred by the Primary Manufacturer, defined as the manufacturer that owns the NDA or BLA for the selected drug, to include: basic pre-clinical research costs, post-investigational New Drug (IND) application costs, completed FDA-required phase IV trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. We are concerned that CMS's proposed information collection overlooks certain investments critical to drug development.

First, by focusing solely on R&D expenditures made by the Primary Manufacturer, CMS's proposed definition overlooks contributions made by the Secondary Manufacturer and others. Drug development is often a collaborative process, involving investments by both small biotech companies and larger pharmaceutical companies. This can take the form of licensing arrangements, co-promotion agreements, and other arrangements. By looking only at the expenditures made by the manufacturer that holds the NDA/BLA, CMS is ignoring a large portion of R&D costs. We also note that his approach is not supported by the statute, which looks at research costs of the "manufacturer," a term that's defined quite broadly to refer to:

> *any entity which is engaged in—*
> *(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or*
> *(B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.*[2]

CMS should therefore collect information regarding R&D spend from across the innovation ecosystem. However—contrary to the approach outlined in the ICR Form—it should not be the responsibility of the Primary Manufacturer to collect this information from Secondary Manufacturers or others. Not only is

[2] Social Security Act (SSA) § 1191(c)(1) (referencing SSA § 1847A(c)(6)(A), which in turn references SSA § 1927(k)(5)).

there no statutory basis for this approach, Primary Manufacturers generally lack access to information regarding the business operations of other manufacturers, and requiring companies to share this sensitive information amongst themselves would add burden and create legal risk. CMS should instead use the ICR Form to solicit information regarding R&D costs from each manufacturer, including Secondary Manufacturers.

In addition, CMS's proposed definition for abandoned or failed drug costs suggests the agency will consider failed or abandoned product costs only for products with some relation to the selected drug at issue (i.e., same active moiety, active ingredient, mechanism of action and therapeutic class). Although these categories capture many of the costs incurred in the development of a given drug, MassBio urges CMS to clarify that it will also solicit information from manufacturers regarding R&D costs for abandoned and/or failed research *that is not attributable to any particular product* across a manufacturer's selected drugs. Developers often incur significant costs in the early stages of the pre-clinical discovery and development process that may not be tied to any particular product, but that were instrumental in moving the needle of scientific discovery forward and laying the groundwork for subsequent innovations that do lead to life-saving therapies. This aspect of R&D is a vital component to the larger process, and should be a material factor considered by the agency.

II. MassBio supports the solicitation of information from the public, in particular patients and providers, but recommends making the submission process less burdensome.

As noted above, the IRA requires CMS to consider certain data on alternative treatments to a selected drug as part of the Negotiation Program. While the statute does not specify where these data come from, CMS is proposing to allow for optional submission from Primary Manufacturers and the public. CMS also proposes to review existing literature, conduct internal analyses, and consult subject matter and clinical experts.

MassBio strongly supports the collection of information from both manufacturers and the public at large regarding the negotiation factors set forth in section 1194(e)(2) of the Social Security Act. The public, in particular patients and providers, have first-hand experience receiving, furnishing, and prescribing selected drugs and it is essential that CMS consider their views on the value of a selected drug and its therapeutic alternatives as part of the negotiation process.

However, we are concerned that requiring the public to register via the HPMS system in order to submit this information is likely to significantly increase the burden on the public of submitting this information, and may deter robust participation in this process. We therefore recommend that CMS allow the public to submit information either via a general email inbox or by using a simple online form that does not require pre-registration.

III. To better compare selected drugs to their therapeutic alternatives, CMS should solicit information regarding key pharmacological dimensions and patient-centered impact.

Question 41 of the ICR Form asks for information on the following with respect to a selected drug relative to existing therapeutic alternatives: therapeutic impact; therapeutic advance; differences in safety profile; and current costs. In terms of therapeutic impact, CMS is looking at health outcomes, surrogate endpoints, intermediate outcomes, patient-reported outcomes, and patient experience. CMS is requesting this information on an indication-specific basis, as applicable.

As a threshold matter, we note that MassBio supports CMS's proposal to collect this information on an indication-specific basis. Given that each drug has a unique set of indications, it is generally the case that the indications for a selected drug will not entirely overlap with the indications with any of its therapeutic alternatives. Moreover, a given selected drug may have a differential therapeutic impact across indications. However, it is essential that CMS consider as potential therapeutic alternatives only those products with the same on-label indications that are actually used in clinical practice as alternatives for that indication. This approach would help ensure that CMS is comparing apples to apples and considering only products and indications for which there are sufficient data. We also urge CMS to provide transparency regarding the therapeutic alternatives it is considering before soliciting information on whether those are the correct therapeutic alternatives, as well as how those therapeutic alternatives compare to the selected drug.

We further urge the Agency to provide further guidance to manufacturers and the public regarding the information CMS is collecting to assess whether a selected drug can be appropriately compared to any proposed therapeutic alternatives in terms of both therapeutic impact and advance. For one, CMS should solicit information that appropriately distinguishes the selected drug and any proposed therapeutic alternatives in terms of key pharmacological dimensions. For instance, CMS should solicit information on the extent to which a given therapy is uniquely suited to treat specific conditions. For example, small-molecule drugs, in particular, are able to effectively accomplish delivery across the "blood-brain barrier," which is essential for the treatment of many mental health conditions.

To aid its determination of therapeutic advance and comparative effectiveness, CMS should also solicit and prioritize information on the ability of a selected drug to assist patients with respect to other important patient-centered measures, including the ability of patients to function and be independent. This is particularly important for therapies that treat debilitating disorders, such as rare disease, for which improvements in function translate into enormous improvements to quality of life. We do not, however, believe that CMS should be comparing drugs to non-pharmacologic interventions, as both treatment types are often used in tandem and thus should not be subject to comparison as alternatives. Accordingly, MassBio supports that CMS has solicited information regarding only pharmacologic therapeutic alternatives, and urge CMS to retain this framework for future initial price applicability years beyond 2026.

IV. In assessing the impact of a selected drug on specific populations, CMS should specifically solicit information on the impact on rare disease and mental health, and should take additional steps to ensure that QALY data are excluded from consideration.

Question 42 of the ICR Form asks questions regarding what is known about the comparative effectiveness of a selected drug with respect to specific populations such as individuals with disabilities, the elderly, the terminally ill and children. It also asks if there are other specific populations not noted that should be considered, and what is known about comparativeness effectiveness of the selected drug with respect to these populations.

In collecting information on the impact of therapies on specific populations, CMS should specifically note that it is collecting comparative effectiveness information regarding issues specific to rare disease populations and individuals with mental illness. These are populations that generally lack access to adequate therapeutic options, and for whom the value of a new therapy is particularly critical. For instance, for rare disease, health utility and services research and data are limited given small populations

and specialized knowledge base, and where there is an on-label therapy for a rare disease, it is often either the first on-label therapeutic option, or the first such option to be approved in decades.

MassBio strongly supports CMS's efforts to exclude information that treats extending the life of individuals in these populations as of lower value, for example certain uses of QALYs, in the negotiation process. This policy aligns with prohibitions set forth in statute, and will help ensure that CMS is not evaluating the value of a given therapy in a manner that discredits its benefit to the neediest and most vulnerable populations. However, we are concerned that certain data sources that violate this prohibition in a discrete way, for example, by describing the research methodology without use of the term "QALY," or by including a QALY analysis as a component of the research methodology without disclosing as much may nonetheless be submitted to CMS. MassBio therefore recommends that CMS disclose to manufacturers, as part of the negotiation process, all evidence that was considered by CMS in developing the initial MFP offer. A manufacturer can then use that information to ensure that any such data that involves QALYs and other similarly problematic metrics—either directly or indirectly—are not included in the manufacturer's counteroffer.

V. CMS should broaden its definition of unmet need, with a lens specific to health equity, and consider whether a selected drug addresses an unmet need on an indication-specific basis.

Question 43 of the ICR Form asks questions regarding whether a given selected drug addresses unmet medical needs. CMS is proposing to define a drug or biologic that meets an unmet medical need as "[a] drug or biologic that treats a disease or condition in cases where very limited or no other treatment options exist…." The instructions and only question for this section focus solely on whether the selected drug and its therapeutic alternatives address an unmet need. MassBio is concerned this question will not provide CMS with the full picture of whether a product has addressed an unmet need.

First, the question fails to consider gaps in therapeutic options *at the time the product was launched*. The ICR Form should thus solicit specific information on the historical context surrounding the selected drug and its therapeutic alternatives in assessing whether the therapy addresses an unmet need.

Second, the question inquires about unmet need generally, and without express consideration of the various indications for the selected drug. CMS should also enhance the quality and utility of the information to be collected by expressly soliciting information as to whether a selected drug meets an unmet need on an indication-specific basis, as it proposes to do for other aspects of its information solicitation.

Third, by focusing solely on the availability of other treatment options, CMS's definition of "unmet medical need" is far too narrow. This narrow definition will serve only continue to disincentivize further biopharmaceutical innovation, especially in these critical areas of unmet need. We recommend that CMS instead look to the FDA's definition outlined in its "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics." Under the FDA guidance, "[a]n unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs)."

Relatedly, CMS should also solicit and prioritize information that views unmet medical needs through the lens of advancing health equity and reducing health disparities by improving access to care among any

underserved communities, including those with high unmet need such as rare disease. In this vein, CMS should solicit information and place greater weight on the ability of the selected drug to treat patients in underserved populations. For example, in the solicitation process, CMS can highlight information on drugs that are able to treat later stages of cancer, as these drugs will disproportionately benefit vulnerable patients from underserved communities who, because of access and related issues, are often diagnosed at later and more advanced stages of disease.

VI. Conclusion

MassBio thanks CMS for your consideration of our comments. As the IRA will have a significant impact across our diverse membership, we would appreciate the opportunity to meet with CMS to discuss these comments and other IRA-related issues of interest to our members.

Best regards,

Kendalle Burlin O'Connell, Esq.
CEO & President
MassBio

NATIONAL HEALTH COUNCIL

May 22, 2023

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd
Baltimore, MD 21244

Re: Agency Information Collection Activities: Proposed Collection; Comment Request

Dear Administrator Brooks-LaSure:

The National Health Council (NHC) thanks the Centers for Medicare & Medicaid Services (CMS) for the opportunity to comment on Information Collection Request (ICR) on data elements for the drug price negotiation process established by the Inflation Reduction Act (IRA).

Created by and for patient organizations over 100 years ago, the NHC brings diverse organizations together to forge consensus and drive patient-centered health policy. We promote increased access to affordable, high-value, equitable, and sustainable health care. Made up of more than 155 national health-related organizations and businesses, the NHC's core membership includes the nation's leading patient organizations. Other members include health-related associations and nonprofit organizations including the provider, research, and family caregiver communities; and businesses and organizations representing biopharmaceuticals, devices, diagnostics, generics, and payers.

As a representative of patient advocacy organizations that are likely to be participating in this data collection process, we are committed to working with CMS to implement the negotiation process in a way that encourages data submission that is meaningful, efficient, and transparent. Our comments are designed to encourage the active involvement of patients and patient advocates in submitting data about selected drugs and their therapeutic alternative(s).

Patient Involvement in Data Submission

Following are some of the comments we submitted in response to the CMS initial guidance on implementing negotiation that are related to data submission by patients and patient advocates. We reiterate them here to stress their importance.

External Data Submission Timing

The NHC understands the tight timeline for the drug selection and price negotiation processes. However, for patients to fully realize benefits of the negotiation program and

to limit unintended consequences, CMS must provide ample time for patients to share data and experiences pertaining to selected drugs. The NHC is concerned that 30 days to submit data after CMS releases the list of drugs to be negotiated is insufficient time for organizations, who do not have research and/or data analysis departments and staff, to collect information and submit data that is most beneficial to CMS. We ask CMS to take the burden of data collection and submission into account as it evaluates the proposed timeframe for data submissions.

The NHC believes CMS should extend the timeframe for stakeholders to submit requested data. At a minimum, the NHC requests that information can still be submitted throughout the negotiation process and could inform "second/final offer" decisions. CMS must consider the patient voice and perspective as vital to the negotiation process.

Engaging Patients to Holistically Consider Therapeutic Alternatives

The NHC appreciates that CMS will consider evidence about alternative treatments to the selected drug, specifically on the categories included in the statute and identified in the guidance, including whether it is a therapeutic advance, FDA approval, effects on specific populations, and addressing unmet needs.

While we understand CMS must adhere to the requirements of the statute, we feel the approach taken in the previous guidance may represent a very narrow interpretation and could be re-defined in a way that takes a more holistic view to determine patients' views on the value of drugs compared to their alternatives. For example, the narrow definition used for "unmet need" could result in misalignment between CMS' and patients' views on the value of the drugs and their therapeutic alternatives. CMS is required to consider evidence about therapeutic alternatives to the selected drug, as available. This includes whether it represents a therapeutic advance; prescribing information; comparative effectiveness, including effects on specific populations; and whether it addresses an unmet need.

We encourage CMS to consider what evidence may be needed for each identified category and support the broadest scope of evidence that may be considered. For example, when considering whether a product represents a therapeutic advance, it is important to consider whether the advance is based on outcomes important to patients, including non-clinical outcomes such as productivity or independence. The patient community is well suited to collect and provide this type of information. A more thorough approach to patient engagement will help CMS better understand a range of elements important to patients to help direct patient organizations toward data that will best suit CMS' needs.

In addition, it will be important for CMS to provide clarity on how it evaluated evidence. When CMS reviews therapeutic alternatives, there should be a clear description of what data was considered and how it influenced the final outcome. The goal of this information should be to demonstrate how patient benefits and clinical appropriateness influenced the final decision.

Patient Engagement and Utilizing Patient Experience Data

The NHC urges CMS to prioritize patient experience data among the many factors the Agency identifies in the guidance as sources that will inform an initial/final offer. Specifically, CMS should ensure that among the data sets that inform any initial or final offer, patient experience data should have an outsized impact as compared to other factors such as research and development costs. CMS should also articulate how patient experience data influenced initial and final offers.

The NHC has long championed the incorporation of patient perspectives in medical product research, development, and coverage. Patient engagement is an important step to better understand the burden of their condition, desired treatment outcomes, and views on benefits and risks. Driven by the work of the Food and Drug Administration on patient-focused drug development (PFDD), many companies in the biopharmaceutical community have devoted significant resources to better understand patient populations and are working to bring to market products that best suit their needs. While patients will benefit from lower-priced medicines, it is important for CMS to consider the positive impact it can have on PFDD if companies are rewarded for demonstrating that their products represent therapeutic advancements over other products and meet unmet needs identified as the most important to patients.

In addition to our previously mentioned concerns about the short timeframe for data submissions, we ask CMS to provide more clarity on how the agency intends to leverage negotiation data elements outlined in the previous guidance to ensure that the agency is evaluating these elements with the patients' experiences, preferred outcomes, and needs in mind. For instance, we ask CMS to transparently outline a consistent methodology for how data related to therapeutic alternatives will result in changes to an initial or final offer. As part of this methodology, we ask that CMS ensure data explicitly related to patient value is prioritized. We also ask CMS to emphasize patient experience and value in the evaluation of data.

We applaud CMS's reference to patient experience in its discussion of the clinical benefits of selected drugs and their therapeutic alternatives in the previous guidance. Defining patient experience in this context and appropriately translating it to a drug's MFP is incredibly important. The NHC urges CMS to consider the following six domains of patient-centered engagement and methodological practices as included in the NHC *Rubric to Capture the Patient Voice: A Guide to Incorporating the Patient Voice into the Health Ecosystem.* The rubric was designed through a multi-stakeholder process to elevate meaningful patient engagement and ensure patient voice inclusion is seen in studies and that engagement includes:

- Patient Partnership;
- Transparency;
- Representativeness;
- Diversity;
- Outcomes Patients Care About;

- Patient-Centered Data Sources and Methods; and
- Timeliness.

Additionally, the NHC urges CMS to prioritize patient experience and patient experience data among the many factors the Agency identifies in the guidance as sources that will inform an initial/final offer. Specifically, CMS should ensure that among the data sets that inform any initial or final offer, patient experience data should have an outsized impact. CMS should also articulate how patient experience data influenced initial and final offers.

Specific Comments in Response to ICR

The NHC recommends that the category of trade association and patient advocacy organization be separated into two categories in question 39. It is important that data from patients and patient advocates be in its own category in order to help the Agency evaluate and prioritize patient-centered data. The types of research and the weight given to different responses may vary greatly between a patient advocacy organization and a trade association representing providers or manufacturers.

In addition, we recommend that the guidance include a definition of patient advocacy organization that makes it clear who qualifies in this category. An example can be found in the National Health Council's Glossary of Patient Engagement Terms - National Health Council:

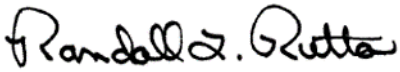
- **Patient advocacy organization:** a 501(c)(3) organization that has a mission to combat a particular disease, disability, or group of diseases and disabilities, or to improve and protect the health of a particular group of people. It engages in programs, such as research, education, advocacy, and service to individuals and communities. It takes a holistic view of the conditions for the patients it represents and seeks universal support from stakeholders for its mission and programs. While a patient advocacy organization may advocate for patient access to care, they do not have prescribing authority; formulary control, responsibility, or decision-making authority; or make drug purchases.

Finally, in the questions regarding evidence about alternative treatments, respondents are asked to certify that the evidence provided does not rely on discriminatory approaches. In the previously issued guidance, CMS stated that they would exclude QALY metrics from data that otherwise factor in QALYs. The NHC appreciates CMS' adherence to the statute and the decision to separate out and exclude such data. However, we are concerned that there may be a lack of clarity among patient groups about this process of utilizing studies that use QALY-related data from secondary sources. This may result in hesitancy to submit certain analyses that are otherwise helpful in establishing the value of a drug or lack of certainty that QALYs have been effectively eliminated from CMS' decisions. Therefore, the NHC requests that CMS offer more clarity into exactly how patients and patient advocates should analyze QALY-based metrics in value-based decisions. This clarity will help patients and patient advocates better respond to the required certification.

Conclusion

The NHC thanks CMS for the opportunity to provide input on this important issue. Please do not hesitate to contact Eric Gascho, Senior Vice President of Policy and Government Affairs, if you or your staff would like to discuss these comments in greater detail. He is reachable via e-mail at egascho@nhcouncil.org.

Sincerely,



Randall L. Rutta
Chief Executive Officer

National
Multiple Sclerosis
Society

May 19, 2023

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Blvd.,
Baltimore, MD 21244

Meena Seshamani, M.D. Ph.D
CMS Deputy Administrator & Director of the Center for Medicare
Department of Health & Human Services
Centers for Medicare & Medicaid Services
7500 Security Blvd.,
Baltimore, MD 21244-1850

RE: CMS-2023-0043-0001

Submitted online via www.Regulations.gov

Dear Administrator Brooks-LaSure and Dr. Seshamani:

Thank you for the opportunity to submit public comments related to the Information Collection Request (ICR) Form for Negotiation Data Elements under sections 11001 and 11002 of the Inflation Reduction Act (IRA). The National Multiple Sclerosis Society (Society) is pleased to offer our feedback and comments relating to the ICR, as these forms are an important piece of the negotiation process. As we have stated in our initial comment on the initial IRA guidance, we applaud the Centers for Medicare & Medicaid Services (CMS) for soliciting public feedback and creating a pathway for public input. The Society looks forward to partnering with CMS to ensure that people with MS can access the medications they need to live their best lives and that medications, and the process for getting them, are affordable, simple, and transparent.

Multiple Sclerosis (MS) is an unpredictable disease of the central nervous system. Currently, there is no cure. Symptoms vary from person to person and may include disabling fatigue, mobility challenges, cognitive changes, and vision issues. An estimated 1 million people live with MS in the United States. Early diagnosis and treatment are critical to minimize disability. Significant progress is being made to achieve a world free of MS.

The Society, founded in 1946, is the global leader of a growing movement dedicated to creating a world free of MS. The Society provides global leadership and funds research for a cure, drives change through advocacy, and provides programs and services to help people affected by MS live their best lives. To fulfill this mission, we fund cutting-edge research, drive change through advocacy, facilitate professional education, collaborate with MS organizations around the world, and provide services designed to help people affected by MS move their lives forward. Additionally, the Society sees itself as a partner to the government in many critical areas. While we advocate for the government's involvement in accelerating the discovery, development, and delivery of new treatments, we do it as an organization whose research investment exceeds $1 billion to date.

The Society is committed to working with CMS to ensure that the drug pricing negotiation program is a success. We believe that for CMS to remain able to cover truly innovative treatments as they come to market, the Agency needs to be able to retain savings from the negotiation process for drugs that are well past their exclusivity period and whose manufacturers have had time to enjoy profits and recoup investments for research and development. While this process represents a change in the U.S. pharmaceutical drug pipeline, we believe it is a necessary one, as the status quo is not sustainable, especially for MS treatments. Our comments on the guidance are informed by the Society's Access to High Quality MS Healthcare Principles and our Access to MS Medications recommendations, which form the basis of any policy related to access, pricing, or coverage of MS treatments.

Information Collection Request Form for Negotiation Data Elements for Primary Manufacturers
We applaud CMS for the scope and detail provided in the ICR form on the factors that will serve as a basis for negotiation and determining the offer and counteroffers from CMS through the negotiation process. We believe that the information on the non-Federal average manufacturer price that is asked for from the primary manufacturer and directions that CMS provides in the ICR form instructions are clear and will provide the agency with the information it needs to inform the negotiation process.

Research & Development Costs and Recoupment
The Society recommends adding a section within Section C, "Research & Development Costs and Recoupment", that allows the primary manufacturer to specify the costs of ongoing research and development to drive improvements and tweaks to existing products to improve the safety, efficacy, or improve side-effects or patient-reported outcomes, even if these outcomes do not make it into the product label. We believe this addition will ensure that primary manufacturers are able to detail and not be penalized for work that is ongoing to improve a treatment or reduce incentives to pursue patient-reported outcomes or clinical outcomes that are important to patients. We believe it is important that this work be captured in the initial offers, counteroffers, and the final negotiated price.

Evidence About Alternative Treatments
The Society appreciates CMS providing a way that members of the public, patient organizations, and others (including secondary or primary manufacturers) can submit feedback and evidence regarding alternative treatments to CMS to inform the negotiation process. While we understand the rationale of requiring all stakeholders to use the same form to submit data to CMS about alternative treatments, we do not believe that the form utilized by the primary manufacturer is appropriate for patients. We recommend that CMS work with representatives from the patient community to develop a form that is more suitable to solicit information from patients and external stakeholders.

Timeline for submitting data on alternative treatments for stakeholders other than the primary manufacturer.
In our initial comment on CMS on the initial drug pricing memorandum, we urged CMS to extend the timeline that patients and patient organizations must submit data about alternative treatments. In examining the elements within the ICR, we reiterate our request that CMS extend the 30-day period to submit data after the list of drugs is selected for negotiation, as this will be insufficient for patients and patient groups to be able to submit the type of data that CMS is looking for to inform their work. Additionally, as there is no statutory obligation to include external data, we do not believe that this type of data submission needs to be bound to the requirements of the primary manufacturer.

We recommend that CMS provide a minimum 60-day period to submit data to inform the negotiation

process as a part of their patient engagement process. This recommendation aligns with our experience providing information regarding the patient perspective and patient journey to the Institute for Clinical Effectiveness and Review (ICER). Additionally, we recommend that the Agency evaluate the access and pricing information that impacts patients during the timeframe of the negotiation. As access and pricing are not stagnant, circumstances may change during the negotiation black-out period that may require additional information on the patient experience or journey, and we urge CMS to remain open to hosting patient listening sessions to fill data gaps after the period for data submission has ended.

Utilization of Patient Experience Data

In previous comments, the Society has urged CMS to prioritize the data that patients submit and patient experience data that is submitted by patient advocacy organizations as it determines the initial, counteroffers, and the final offer for maximum fair price (MFP). Additionally, we have urged CMS to detail how this type of data influenced the MFP and what types of data were helpful to inform the decision. We believe this will help stakeholders understand what types of information were useful to CMS in their decision-making.

As stated above, if CMS de-links the statutory timeline for data from primary manufacturers, it will give additional time and opportunity for CMS to gather important patient experience data that could be modeled from work done at the Food and Drug Administration's Patient-Focused Drug Development work.

Discriminatory Metrics in the Negotiation Process

As discussed in our previous comment, the Society believes that cost and comparative-effectiveness methodologies cannot accurately measure value if they do not include the patient experience, preferences, and outcomes. To promote high value healthcare and ensure quality outcomes for Medicare beneficiaries any measure being used in healthcare decision-making should accurately capture the complex lives of people living with disabilities and not undervalue their lives or experience. For this reason, we appreciate calling out that stakeholders should not include data that utilizes the Quality-Adjusted Life-Year (QALY), which treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill in the negotiation process; however, we are concerned that patients and some patient groups may not realize that information they submit utilizes these metrics, so we urge CMS publish the list of resources that utilize these metrics and note why that resource was not used. As the first year of negotiation will be a learning experience for all involved, we believe CMS identifying why a particular resource was not utilized will help all stakeholders understand the parameters in which CMS will utilize certain resources and why others are excluded during the negotiation process. Additionally, we reiterate our request from previous comments that CMS take the opportunity to begin work on a novel metric that lacks the discriminatory impact of the QALY.

Certification of Submission for Respondents Who Are Not Primary Manufacturers

The Society believes that stakeholders who submit data to CMS to inform the negotiation process should have to certify that the information they are submitting is correct to the best of their knowledge. However, we do not believe that the current attestation for stakeholders who are not primary manufacturers is appropriate for patients or patient organizations. We are concerned that the current language would dissuade stakeholders from submitting useful information because of the concerns around liability. To ensure that stakeholders are comfortable submitting data, we urge CMS to bring

together representatives from patient groups to work on language that meets the needs of CMS and is better aimed at soliciting data on alternative treatments from this population.

Additionally, we urge CMS to include language that would ensure that stakeholders are not submitting data or information that is from a primary or secondary manufacturer. We are concerned that, as written, there is no guardrail that prevents a third party from submitting data/information on behalf of a manufacturer of a treatment.

Ensuring Robust Patient Engagement

In our previous comment on the CMS guidance, we recommended that CMS engage patient groups and the patient community often as it works through the process that will inform the initial price applicability year of 2026 and beyond. After reviewing the elements of the ICR and having a better understanding of the expectations that will be placed on patients and patient groups during the data submission process, we reiterate this request to ensure that CMS has a formal process that all stakeholders- but particularly for patients and patient advocacy groups- can utilize to ensure the success of the Medicare Drug Price Negotiation program. As the negotiation process matures, it is our experience that a formal process levels the playing field and allows for a better flow of information between the Agency and stakeholders on what elements of the program and process are working and where improvements can be made. The Society believes that formalizing patient engagement in this way will go a long way to build trust in the process and ensure that the Agency hears directly about what elements are most important to patients to help guide conversations about value and cost.

Thank you again for the opportunity to provide feedback on the ICR form and negotiation data elements. If you have any questions about our comments and recommendations, please contact Leslie Ritter, Associate Vice President of Federal Government Relations at Leslie.Ritter@nmss.org.

Sincerely,

Bari Talente, Esq.
Executive Vice President, Advocacy and Healthcare Access
National Multiple Sclerosis Society

National Pharmaceutical Council

1717 Pennsylvania Avenue, NW, Suite 800, Washington, DC 20006 Phone: 202.827.2100 Fax: 202.827.0314 Web: www.npcnow.org

May 22, 2023

Ms. Lara Strawbridge
Deputy Director for Policy, Medicare Drug Rebate and Negotiations
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016

Submitted Electronically via: http://www.regulations.gov

RE: CMS–10847 Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act

Dear Deputy Director Strawbridge:

The National Pharmaceutical Council (NPC) appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS) Notice, *CMS–10847 Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act* (ICR or the ICR).

NPC is a health policy research organization dedicated to the advancement of good evidence and science and to fostering an environment in the United States that supports medical innovation. We have rich experience conducting research and disseminating information about the critical issues of evidence, innovation and the value of medicines for patients. Our research helps inform important healthcare policy debates and supports the achievement of the best patient outcomes.

NPC's research and that of others have found that public policies that reduce the incentives to invest in research and development result in less innovation, fewer treatment options, and lower life expectancy.[1] The Inflation Reduction Act (IRA) creates a new price-setting mechanism that will change the economic incentives for bringing new medicines to market, and evidence

[1] Ciarametaro M and Buelt L. Assessing the effects of biopharmaceutical price regulation on innovation. 2022. https://www.npcnow.org/resources/assessing-effects-biopharmaceutical-price-regulation-innovation; Thomas A. Abbott & John A. Vernon, 2007. "The cost of US pharmaceutical price regulation: a financial simulation model of R&D decisions," Managerial and Decision Economics, John Wiley & Sons, Ltd., vol. 28(4-5), pages 293-306; Leonard D. Schaeffer Center for Health Policy & Economics. Annual Report 2020. https://healthpolicy.usc.edu/wp-content/uploads/2021/03/Schaeffer-Center-2020-Annual-Report.pdf

suggests manufacturers are already responding to those incentives.[2] The importance of implementing the price-setting provisions of the IRA in a manner that accurately values medicines and maintains patient access cannot be overstated. This new process forces manufacturers to accept CMS's final price, face an unreasonable excise tax, or exit the market – all of which threaten the development of, and patient access to, new treatments or cures.

We appreciated the opportunity to provide input on the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance). We further appreciate the opportunity to comment on the ICR and encourage CMS to use discretion in designing the Negotiation Data Elements information collection in a way that neither inappropriately burdens manufacturers nor constrains the ability of stakeholders to fully communicate relevant information in the context of a transparent drug evaluation process. Specifically, NPC makes the following recommendations:

1. Increase Transparency and Flexibility around CMS's Process.
2. Reduce Manufacturer Burden While Removing Inappropriate Constraints.
3. Clarify and Expand Patient-Centered Data Elements on the Value of Treatments.
    a. Specifically recognize the voice of caregivers and patient advocacy organizations (Question 39).
    b. Encourage respondents to provide rationale for their choice of therapeutic alternatives (Questions 40-43).
    c. Collect clarifying information on how submitted evidence has been separated from QALYs (Questions 40-43).
    d. Expand outcomes to consider surrounding Therapeutic Impact and Comparative Effectiveness (Question 41).
    e. Expand definition of unmet need (Question 43).
    f. Expand opportunities for patients and caregivers to describe preferences and priorities.

<u>Increase Transparency and Flexibility around CMS's Process.</u>

This form, even in combination with the Guidance, provides limited insight into how CMS will evaluate drugs, or the factors considered during the price-setting process. With more information on the decision-making framework, respondents can better structure their data responses to include relevant information for CMS's evaluation. More robust information about the evaluation criteria also builds trust in the price-setting process and would improve the

[2] Grogan J. (2022) The Inflation Reduction Act Is Already Killing Potential Cures. WSJ. https://www.wsj.com/articles/the-inflation-reduction-act-killing-potential-cures-pharmaceutical-companies-treatment-patients-drugs-prescriptions-ira-manufacturers-11667508291 Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions; Powaleny, Andrew. (2023). IRA Impacts: Cancer treatment research and development. PhRMA. Available at: https://catalyst.phrma.org/ira-impacts-cancer-treatment-research-and-development; Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions; IRA survey: Biotechs bracing for impact. Biocentury. March 16, 2023.

utility of data submitted. We therefore strongly encourage CMS to specify how the data elements will be used in its price-setting process. We further encourage CMS to consider revisions to the Negotiation Data Elements questions in the context of creating a transparent, robust, and replicable framework based in scientific principles for their drug evaluation process, enabling manufacturers and other stakeholders to submit data that will meaningfully inform the drug evaluation process. Because public submission comes with a cost of sorting through and identifying studies that are both high quality and relevant, we recommend CMS make public the procedures by which evidence is identified and included in its assessments. Transparent standards informed by accepted rubrics for evaluating the quality of studies based on diverse data sources, including clinical trials, patient registries, and other real-world data, will promote the use of methodologically rigorous evidence in the evaluation process. While we encourage transparency in evidentiary standards and evaluation processes to build credibility and trust in the process, we also note the utmost importance of maintaining confidentiality of proprietary information. We encourage CMS to state clearly how proprietary data will be stored, accessed, and protected to ensure confidentiality.

CMS's framework for drug evaluation and the Negotiation Data Elements questions would further benefit from flexibility that promotes a collaborative approach to information exchange. Stakeholders should be given opportunities to provide comprehensive evidence on drug value, including information on non-statutory factors and new evidence as it becomes available. Additionally, flexibility in the Data Negotiation Element questions would better accommodate variable approaches across the industry to characterizing data elements, including development programs, which may lead to inappropriate comparisons and assessments. NPC urges CMS to provide greater flexibility in the ability of broad stakeholders to communicate evidence and meaningfully engage with the evaluation process. Constraining diverse stakeholders to a rigid, one-size-fits-all approach to providing evidence limits the robustness of stakeholder engagement and the evaluation process.

Reduce Burden While Removing Inappropriate Constraints.

In its implementation of the IRA, NPC urges CMS to focus on clinical benefits and cost offsets when comparing treatments and determining value, and not to reduce the preliminary price by information unrelated to the value of a treatment (e.g., cost-recovery, remaining exclusivity, etc.). We recognize that under the IRA statute [1194(e)(1)], the Secretary shall consider manufacturer-specific information during the price-setting process, including research and development costs and their recoupment, market data for the drug, unit costs of production and distribution, and Federal financial support. However, the ICR questions soliciting manufacturer-specific data are misaligned with a drug evaluation process focused on the value of treatments. Further, many questions introduce considerable response burden. To respond to the in-depth and specific questions on research and development costs, unit costs, and market data with both accuracy and clarity requires more time and space than is allotted through the current ICR. For example, historical development costs for products approved over seven years ago may easily date back two decades. Given our recommendation that CMS should not reduce the preliminary price by information unrelated to the value of a treatment to US patients and

health systems, as well as the logistical burdens and feasibility concerns surrounding the questions in Sections C (Research and Development), D (Unit Costs of Production and Distribution), and G (Market Data, Revenue, and Sales Volume Data), we encourage CMS to limit the *required* submission of elements in these sections.

While many required Negotiation Data Elements questions, particularly those outlined in the IRA statute in 1194(e)(1), are unduly burdensome, others, notably those in Section H that relate to the elements in the IRA statute in 1194(e)(2), inappropriately constrain stakeholders' ability to fully communicate information relevant to the drug evaluation process. Principles of good comparative effectiveness research – as well as the practices and policies of other payers and regulators - include robust stakeholder engagement. Given their vast knowledge of their products and therapeutic areas, pharmaceutical manufacturers and their pharmacoeconomic researchers are critically important sources of information on the value of treatments for payer decision-making. The ability of stakeholders to communicate relevant information should not be constrained by arbitrary and limited word counts. For example, patient-centered unmet medical needs are multifaceted and may reflect patient preferences, heterogeneity in response to existing treatment options, and improvements in benefits not captured in conventional measures of health gain (e.g., caregiver benefit, equity, and patient dignity).[3] Despite this, Question 43: Addressing Unmet Medical Needs in the ICR restricts respondents to only 1000 words. We urge CMS to eliminate restrictive word counts for information collection responses. At a minimum, we encourage CMS to take the time needed to build an informed and rigorous process and methodology, including eliminating these word counts, for initial price applicability year (IPAY) 2026. As information will develop and change over the course of the negotiation process, particularly for IPAY 2026, manufacturers should be given opportunities to supplement their initial responses and have due consideration.

Clarify and Expand Patient-Centered Data Elements on the Value of Treatments.

The ICR ostensibly provides opportunities for manufacturers, clinicians, and patients to provide evidence about the selected drug and alternative treatments. However, the questions, definitions, and word limits in Section H: Evidence About Alternative Treatments limit stakeholders' ability to communicate critical information about the impact and value of treatments. NPC encourages CMS to specifically seek and incorporate feedback throughout the evaluation process from key stakeholders, including patients, caregivers, clinicians, and manufacturers. Regarding the ICR, we urge CMS to:

a. *Specifically recognize the voice of caregivers and patient advocacy organizations (Question 39).* In Section H: Evidence About Alternative Treatments, respondents may check the relevant box which best describes the person completing the form. Options include "representative of a trade association or patient advocacy

[3] Synnott PG, Voehler D, Enright DE, Kowal S, Ollendorf DA. The Value of New: Consideration of Product Novelty in Health Technology Assessments of Pharmaceuticals. Appl Health Econ Health Policy. 2023 Mar;21(2):305-314. doi: 10.1007/s40258-022-00779-0. Epub 2022 Dec 19. PMID: 36529826

organization," and "a patient who has experience taking this drug." Caregivers' views of the benefits of drugs are essential to understanding the full range of clinical and patient-centered outcomes.[4] Caregiver costs and burden are meaningful outcomes that are often poorly captured in existing data sources. We encourage CMS to explicitly recognize the important voice of caregivers by including caregivers as a category of respondent in Question 39. Additionally, we encourage CMS to recognize the unique role of patient advocacy organizations in promoting the priorities and voice of patients by creating a separate category of respondent for these organizations.

b. *Encourage respondents to provide rationale for their choice of therapeutic alternatives (Questions 40-43).* Questions throughout Section H: Evidence About Alternative Treatments solicit information about the selected drug and its therapeutic alternative(s) but does not explicitly ask for feedback on the selection of therapeutic alternatives. NPC recommends that the choice of comparators be driven by clinical appropriateness, informed by current treatment practices among a relevant patient population, and selected from potential comparators with the same treatment modality and class, rather than be dictated by cost, other concerns, or implicit goals. We encourage CMS to prioritize reducing bias in treatment comparisons by identifying therapeutic alternatives from potential comparators with the same treatment modality, class, and mechanism of action and limiting the choice of therapeutic alternative to drugs and biologics with FDA-approved indications. A rapid, multi-stakeholder scoping process beginning immediately after the selected drugs are announced would enable dialogue with manufacturers and other key stakeholders to identify appropriate therapeutic alternatives prior to the public submission process.

c. *Collect clarifying information on how submitted evidence has been separated from QALYs (Questions 40-43).* The ICR includes language surrounding the exclusion of evidence that uses a metric "such as QALYs in a life-extension context" but specifies that in instances where a study has "separated this use of QALYs from other evidence in the report (e.g., clinical effectiveness, risks, harms, etc.) that is relevant to the factors" considered during the price-setting process, "CMS will consider such separate evidence." NPC is mindful of the prohibition against the use of QALYs and encourages CMS to consider patient-reported outcomes that are complete, comprehensive, and fit for purpose, as opposed to limited, utility-based approaches including the QALY and other potentially discriminatory measures. Accordingly, we encourage CMS to specifically ask for information on how submitted evidence has been separated from QALYs.

[4] Patient-Centered Outcomes Research Institute (PCORI). Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. https://www.pcori.org/resources/landscape-review-and-summary-patient-and-stakeholder-perspectives-value-health-and-health-care

d. *Expand outcomes to consider surrounding Therapeutic Impact and Comparative Effectiveness (Question 41).* There are a multitude of specific benefits that constitute the value of a drug, including societal benefits such as patient and caregiver indirect costs, scientific spillover, limiting the fear and risk of contagion for infectious diseases, increasing health equity, and cost offsets. In the CMS Framework for Health Equity 2022-2032, the Agency notes that the framework "challenges [CMS] to incorporate health equity and efforts to address health disparities as a foundational element across all [CMS] work, in every program, across every community."[5] We urge CMS to recognize the importance of increasing health equity as a benefit that constitutes the value of a drug, aligned with the Agency's goal of incorporating health equity in all CMS programs. The information solicited by Question 41 focuses data on a selected drug's therapeutic impact on "health outcomes, surrogate endpoints, intermediate outcomes, patient-reported outcomes, and patient experience." Given the importance of societal value and cost offsets, we encourage CMS to specifically recognize these outcomes in Question 41, including, but not limited to: patient and caregiver indirect costs, scientific spillover, limiting the fear and risk of contagion for infectious diseases, increasing health equity, and cost offsets.

e. *Expand definition of unmet need (Question 43).* The definition of unmet need provided alongside Question 43 is substantially narrower than definitions of unmet need found in the peer-reviewed literature and promulgated by the FDA as well as international agencies.[6,7] We encouraged CMS to expand their definition of unmet medical need in their Guidance to include a multifaceted definition informed by patient and provider perspectives. We similarly urge CMS to update the definition of Unmet Medical Need in the Data Negotiation Elements Questions.

f. *Expand opportunities for patients and caregivers to describe preferences and priorities.* Despite the importance of patient engagement during IRA implementation,[8] the ICR provides limited opportunities for patients and caregivers to describe critical elements of the value of drugs, including:
    - the preferences and priorities that inform shared decision-making between appropriate treatment options;
    - definitions of the benefits that are most important to patients;
    - selection of measures to quantify benefits; and,

[5]Centers for Medicare & Medicaid Services. CMS Framework for Health Equity 2022-2032. https://www.cms.gov/files/document/cms-framework-health-equity-2022.pdf

[6] Vreman RA, Heikkinen I, Schuurman A, et al. Unmet Medical Need: An Introduction to Definitions and Stakeholder Perceptions. *Value in Health*. 2019;22(11):1275-1282. doi:10.1016/j.jval.2019.07.007;

[7] Synnott PG, Voehler D, Enright DE, Kowal S, Ollendorf DA. The Value of New: Consideration of Product Novelty in Health Technology Assessments of Pharmaceuticals. Appl Health Econ Health Policy. 2023 Mar;21(2):305-314. doi: 10.1007/s40258-022-00779-0. Epub 2022 Dec 19. PMID: 36529826

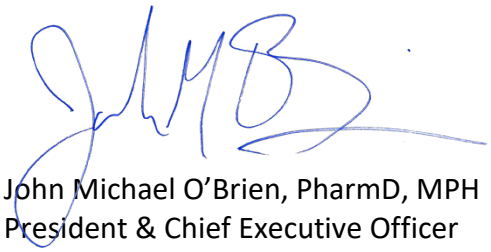
[8] "Patient Engagement & Experience Data: Missing Ingredients For CMS' Successful IRA Implementation", Health Affairs Forefront, May 16, 2023. DOI: 10.1377/forefront.20230515.743661

- patient preference regarding the benefits and risks of a product, its available dosage forms, and innovative delivery systems.

Patient and caregiver engagement is further constrained by the limited word counts and a lack of patient-friendly language. The lack of patient-friendly language creates concerns about the ability of CMS to capture the voices of underrepresented and historically marginalized populations as well as patients with limited health literacy. While this form must be revised to facilitate patient contributions, our recommendation only underscores the need for more robust opportunities for patient and caregiver engagement throughout the evaluation process as we described in our response to the initial Guidance.

The National Pharmaceutical Council appreciates the opportunity to submit comments in response to this ICR and looks forward to ongoing opportunities to engage with CMS as it implements the Medicare Drug Price Negotiation Program. Please contact me at john.obrien@npcnow.org or (202) 827-2080 if we may provide any additional information.

Sincerely,



John Michael O'Brien, PharmD, MPH
President & Chief Executive Officer

May 22, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Meena Seshamani, M.D., Ph.D.
Deputy Administrator and Director of the
Center for Medicare
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Dear Administrator Brooks-LaSure and Dr. Seshamani,

On behalf of the more than 25 million Americans living with one or more of the over 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks the Centers for Medicare and Medicaid Services (CMS) for their extensive engagement with the rare disease community around implementation of the Inflation Reduction Act (IRA). NORD appreciates this opportunity to provide comments on the Information Collection Request (ICR) Form for Negotiation Data Elements under Section 11001 and 11002 of the IRA (CMS-10847), hereafter referred to as the "ICR."

NORD is a unique federation of non-profits and health organizations dedicated to improving the health and well-being of people living with rare diseases. NORD was founded 40 years ago, after the passage of the Orphan Drug Act (ODA), to formalize the coalition of patient advocacy groups that were instrumental in passing that landmark law. Our mission has always been and continues to be to improve the health and well-being of people with rare diseases by driving advances in care, research, and policy.

The IRA will impact rare disease patients' access to therapies in complex ways. For many Americans living with a rare disease, out of pocket prescription drug costs create significant financial barriers and hinder patient access to needed therapies**.** Key provisions in the IRA, including the $2,000 annual and amortized monthly caps on out-of-pocket costs for Medicare Part D beneficiaries, as well as expanded eligibility for financial assistance for low-income beneficiaries, once fully implemented, will ensure that more rare disease patients on Medicare will be able to afford the life-altering therapies they need.

On the other hand, before the Orphan Drug Act was signed into law in 1983, fewer than 40 FDA-approved therapies were available to treat rare diseases.[1] Thanks to the incentives created by the ODA, rare disease therapies now consistently account for more than half of FDA approvals for new molecular entities.[2] Still, more than 90% of the more than 7,000 known rare diseases do not have an FDA approved treatment, making continued investment in rare disease research and innovation especially important to

[1] Orphan Drugs In The United States: An Examination of Patents and Orphan Drug Exclusivity (2021): available at https://rarediseases.org/wp-content/uploads/2022/10/NORD-Avalere-Report-2021_FNL-1.pdf; accessed 4/2023
[2] New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products; available at: https://www.fda.gov/drugs/development-approval-process-drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products; accessed 4/2023

1779 MASSACHUSETTS AVENUE NW, SUITE 500
WASHINGTON, DC 20036
T 202-588-5700 ▪ F 202-588-5701

55 KENOSIA AVENUE
DANBURY, CT 06810
T 203-744-0100 ▪ F 203-263-9938

1900 CROWN COLONY DRIVE, SUITE 310
QUINCY, MA 02169
T 617-249-7300 ▪ F 617-249-7301

rarediseases.org ▪ orphan@rarediseases.org

the rare disease community.[3] The limited exemption for orphan products approved to treat a single rare disease will help encourage this continued innovation, as will the exemption for products with less than $200 million in annual Medicare spending. However, the small patient populations and medical complexity associated with rare diseases create unique challenges to rare disease drug development, and these same complicating factors may also make it more difficult to determine a fair negotiated price for products that treat rare diseases compared to other therapies.

At the same time, therapies that treat rare diseases are often placed on the non-preferred or specialty tiers of Medicare Part D plan formularies and/or are subject to step therapy and other utilization management strategies, resulting in significant out of pocket costs and access delays - and making some therapeutic options virtually inaccessible to many rare disease patients. These policies *de facto* limit which treatment options are feasible alternatives for many rare disease patients. Given these complex factors and their immense impact on patients' lives, NORD appreciates CMS' efforts to capture and incorporate the patient voice in the negotiation process.

To appropriately capture the patient's voice, patient input must be decoupled from this ICR; CMS must be more proactive in engaging the patient community in the data collection. NORD urges CMS to address three specific areas of concern to ensure the rare disease community fully benefits:

1. Decouple and simplify the collection of patient experience data from this ICR.
2. Proactively collect patient experience data through externally–led patient-listening sessions.
3. Engage FDA's and CMS' patient engagement experts as well other relevant government, academic, and private sector experts at every step of the data collection process.

Specifically, CMS should take the following steps to support rare disease patients and families in providing input into the drug negotiation process:

1. Decouple and simplify the collection of patient experience data from this ICR.

The primary purpose of this specific ICR is to facilitate the mandatory collection of manufacturer data, guided by statutory data elements, rigid processes, and tight timelines. The collection of patient experience data is both qualitatively and quantitatively very different from this primary purpose as collecting patient experience data is neither subject to statutory data elements nor does it have to follow the very tight timelines for manufacturer-provided data that would be virtually impossible for most patients to navigate. The type of data elements collected are also different, as evident from the ICR – with the manufacturer data mostly quantitative and clearly defined, capturing highly concrete issues such as a drug's annual sales volume, unit price of production, or patents and exclusivities.

In contrast, the patient-reported data is by design significantly more qualitative and much less precisely defined, capturing issues such as the extent to which a drug provides a meaningful advantage over an alternative therapy, or the extent to which an unmet medical need is not adequately addressed by

[3] Larkindale J, Betourne A, Borens A, Boulanger V, Theurer Crider V, Gavin P, Burton J, Liwski R, Romero K, Walls R, Barrett JS. Innovations in Therapy Development for Rare Diseases Through the Rare Disease Cures Accelerator-Data and Analytics Platform. Ther Innov Regul Sci. 2022 Sep;56(5):768-776. doi: 10.1007/s43441-022-00408-x.

available therapies. In fact, even the key audience for the patient reported data elements is significantly different from the manufacturers, and is likely to include patients and families, health care providers, academic researchers, and other relevant stakeholders. Additionally, the number of individual potential respondents is exponentially higher than for the manufacturer data. As a result, the ICR is unlikely to be an effective tool for capturing patient-reported data.

NORD is concerned CMS' plans to largely rely on this ICR for voluntary data submissions by the public will be unsuccessful. As proposed, the data collection will occur on very short timelines, without meaningful data standardization, using complicated forms written at too advanced reading levels and depending on hard-to-navigate processes that are neither intuitive nor patient-friendly. NORD is specifically concerned that patients will either not become aware of the data collection effort in time, or struggle to navigate the complex submission process. The extent to which individual data submissions will be confidential and protected from disclosure will be confusing to patients, and we worry the burden for patients not familiar with a process that was developed for manufacturers may be significantly higher than estimated, in particular for patients who may navigate additional challenges such as language barriers, visual impairments, or lack of (broadband) internet access. In addition, the required attestations are worded in a way that will likely discourage many patients from submitting data, and to the extent patients will feel compelled to submit data containing Personal Identifiable Information (PII) and Personal Health Information (PHI), the data collection raises privacy concerns.

Moreover, NORD foresees challenges in aggregating and analyzing individual patient and provider experience data submitted through this process; the data will be collected without a sampling frame and likely not representative while the collection method essentially makes it impossible to determine or account for such inherent biases in the data. In addition, the lack of standardized questions and scientific rigor will likely render this data largely anecdotal as opposed to data collected following appropriate qualitative and/or quantitative research methodologies to collect this information in a scientifically rigorous and reproducible manner as is currently done with data collected through the FDA's patient-focused drug development meetings or patient surveys. FDA's Guidance "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input" [4] for instance, provides detailed and tangible guidance on operationalizing and standardizing data collection and data management in a way that works for the rare disease patient community.

For the reasons outlined above, NORD urges CMS to:

a. **Decouple the collection of patient-reported data from the ICR.** As outlined above, the collection of patient data has virtually nothing in common with the mandatory submission of manufacturer data. Decouple the collection of this important patient data from a process that was never meant to collect this type of data - or to engage this number and diversity of respondents.

b. **b. Simplify and streamline the data submission process for patients, caregivers, and providers so that it is workable and does not provide undue barriers to providing the requested information**.

[4] FDA GFI: Patient-Focused Drug Development: Collecting Comprehensive and Representative Input; available at https://www.fda.gov/media/139088/download; accessed 4/2023

Decoupling the process from manufacturer provided data will allow CMS to create a data collection process that is designed to be patient-centered, with input and guidance from patients at every step of the process. This should include pre-testing the forms, attestations, and instructions with representatives of the relevant community to ensure they are clearly understood and easy to navigate, including by individuals with visual and other impairments. Because this data submission is voluntary and not subject to the statutory data submission timeline for mandatory manufacturer-provided data, CMS should work with the patient community to establish feasible timelines that will be workable for the community. Other concerns, such as ensuring the respondents are in fact patients, caregivers, or families afflicted by the disease and report their own experiences and perspectives, will require careful consideration, in close collaboration and with guidance from the patient community. FDA listening sessions, patient-focused drug development meetings, and other FDA-led initiatives routinely navigate these challenges and collect meaningful patient experience data in ways that work for rare disease patients and families and can serve as a valuable guide and resource for CMS, including all applicable attestations and data protections.

c. **Clarify now what information the agency is seeking from patients and in what format to allow data standardization and aggregation.** The short time period outlined for the negotiation process makes it imperative to provide detailed instructions as early as possible, before the negotiation period begins, to facilitate and streamline the collection and submission of meaningful data from a patient perspective. Clarifying the key data elements in sufficient granularity ahead of time will also empower patient advocacy groups and other important stakeholders to proactively collect and collate relevant information in a way that is scientifically rigorous and representative of the relevant patient community.

2. Proactively collect patient experience data through externally-led patient-listening sessions.
NORD thanks CMS for recognizing the unique and nuanced value drugs can bring to specific subsets of the patient population, including rare disease patients who often have few or no therapeutic options. NORD commends CMS' efforts to consider data on clinical benefit, therapeutic alternatives, and unmet medical need in the negotiation process. The agency's stated objective to assess value in an indication-specific manner including some off-label uses, is critical to CMS understanding the complex tradoffs and unmet needs that exist within the rare disease patient community. Moreover, we are encouraged that CMS has explicitly recognized the value of patient experience data, including its nuances, and the expectation that not all patients are necessarily sharing the same views and experiences. For instance, the science of patient engagement has long recognized that patient experience data may reflect differences depending on disease progression or a patient's cultural, geographic, and socio-economic background. While we are grateful CMS recognizes the value of patient experience data, we strongly encourage CMS to expand the opportunities and strengthen the processes for providing such input.

<u>The external data CMS staff plan to rely on in the negotiation often does not exist for most rare diseases, creating an added burden for CMS and the affected community to collect this data.</u> CMS plans to supplement the data submitted by the public through this ICR with relevant published data, relying on such data being readily available to CMS staff through literature searches. Unfortunately, it is a recognized challenge that for many rare diseases, data relevant to determine a negotiated product's clinical benefit, therapeutic alternatives, or unmet medical need often does not currently exist in peer-

reviewed journals or consensus treatment guidelines. FDA's Voice of the Patient (VOIP) reports, which are trying to fill this void, are playing an increasingly important role in patient-focused drug development and frequently collect meaningful information on how patients evaluate therapeutic alternatives or characterize the unmet need and clinical benefit of alternatives. However, these data are not indexed in a way that would clearly find them in a traditional literature search. In addition to ensuring CMS considers all relevant data collected as part of the FDA approval process in the negotiation process, patient and provider engagement will be critical to ensure CMS is aware of and able to leverage all available data. This is particularly important for rare diseases because the lack of disease-specific International Classification of Disease (ICD-10) codes for most rare diseases makes strategies relying on existing real-world data (RWD) from sources such as electronic health records (EHRs) or medical claims data largely infeasible for many rare diseases.

CMS will have to collect data on treatment alternatives, clinical benefit, and unmet medical need for rare diseases *de novo,* including from patients, caregivers, and providers. In fact, patients and caregivers have key insights on issues such as determining the value of a therapy and how it compares to potential alternate treatment options. For instance, rare disease patients are often uniquely positioned to share the challenges associated with unmet medical needs - when there are no or very few options available to treat their condition - and the benefits to themselves, their families, and the community from a safe and effective therapy. Patient experience data will be particularly important given CMS' desire to evaluate price on an indication-specific level including certain off-label uses, which are common in the rare disease space albeit notoriously hard to study.[5] Because published data to assess these specific uses remain scarce, patients and providers are often the best experts from which to elicit such information for the rare disease community.

For the reasons outlined above, NORD urges CMS to:

a. **Partner with key stakeholders on externally-led patient listening sessions specific to selected drugs to collect representative data to inform CMS' initial offer for a negotiated price.**

- In planning these sessions, CMS should use FDA patient listening sessions as a roadmap and work closely with the impacted patient communities to develop a representative and meaningful data collection effort. For instance, while we appreciate CMS' intends to only focus on pharmaceutical alternatives and to primarily consider alternatives in the same drug class, we recognize non-pharmaceutical options such as surgery are often the only viable alternative for our patient populations and that therapeutic alternatives in other drug classes and with other mechanisms of actions may be the most appropriate alternatives for some of our patients.

- Engaging the patient community in planning the listening session will help ensure that these alternatives are appropriately considered. Having external groups take a leadership role can

[5] Fung A, Yue X, Wigle PR, Guo JJ. Off-label medication use in rare pediatric diseases in the United States. Intractable Rare Dis Res. 2021 Nov;10(4):238-245. doi: 10.5582/irdr.2021.01104. PMID: 34877235; PMCID: PMC8630459.

help address both CMS staffing shortages and concerns about administrative and logistical issues (e.g., compliance with administrative and legal requirements for federal data collection).

- Logistically, patient listening sessions will likely be most effective if they focus on one negotiated drug and one (or potentially multiple closely related) uses or indications. This may require prioritization among drugs and indications that will be part of the negotiation program and should be guided by considerations such as to what extent the patient listening session will generate unique data to close key data gaps and to what extent the generated data is likely to materially impact the price negotiation. Transparency and engagement of the stakeholder community in this decision-making will be key to success. In fact, pre-meeting community surveys and enrollment strategies such as snowball sampling, when used appropriately, can be effective in helping to ensure the listening sessions will truly reflect the affected community.

- Other considerations include issues such as ensuring appropriate representation and diversity of perspective among the meeting participants; identifying and prioritizing questions for meeting participants ahead of time to provide time to prepare; carefully designing and pre-testing questions with consideration for well-established heuristics and cognitive biases (e.g., anchoring and adjustment, bandwagon effect, availability); and developing tools and approaches to capture the meeting outcomes in a way that is scientifically valid and allows participants to review the summary. Here again, FDA's experience with patient listening sessions and patient-focused drug development meetings will be able to provide valuable lessons learned.

b. **Include consistent and granular summaries of the data and assumptions on which each negotiation was based, including patient experience data.** We urge CMS to report a detailed and standardized summary of the data relied upon in the negotiation process including the therapeutic alternatives, clinical benefit, off-label use, and unmet need for each indication and the data sources relied upon. CMS should further break out the use of patient experience data and patient-reported outcomes; list data identified by CMS through literature searches and guideline review as well as primary data, such as claims, EHR, or other real-world evidence (RWE), generated and collated by CMS. This level of transparency will be key to create consistency and trust in the negotiation process. Clearly breaking out the use of different data will also motivate the creation of valuable patient experience data for future negotiation years. In fact, much of the data for rare diseases collected through this process will be unique and useful beyond this specific negotiation process.

3. Engage FDA's and CMS' patient engagement experts as well other relevant government, academic, and private sector experts at every step of the data collection process.

NORD recognizes that the timelines for the IRA implementation are exceedingly short. Fortunately, as CMS engages on capturing patient perspectives in the Negotiation Program, the agency can draw upon a rich set of existing data, relevant scientific knowledge, and experience. For instance, considerable deliberation and research has gone into defining and measuring key concepts such as unmet medical need or therapeutic advantage.[6] Rather than reinventing these concepts, CMS can draw upon decades

[6] https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

of practice in the FDA space to streamline and fast track the process. Similarly, the science of patient engagement has made tremendous progress in the past decade. The academic literature is full of scientific studies seeking to identify best practices, develop tools to streamline the process, and capture the value of patient engagement. In fact, a 2014 systematic review of patient engagement in research identified 142 studies that met the inclusion criteria[7] – and hundreds more studies have been published in the decade since. FDA has made leaps in developing patient engagement best practices and tools that are largely applicable across FDA's product centers and through every step of the product life cycle.

CMS itself has a long history of successfully engaging patients and families. Tools such as CMS' Person and Family engagement strategy[8] have been instrumental in empowering patients and families to be meaningful partners in the design, delivery, and evaluation of their care. NORD also brings a wealth of experience engaging patients in various parts of the drug development and reimbursement space, and a range of other non-profit and academic institutions from the Patient-Centered Outcomes Research Institute (PCORI) and the Milken Institute's FasterCures Center to the Medical Device Innovation Consortium (MDIC) to a range of more disease-specific patient groups and many, many, others will have meaningful advice to offer. Relying on this wealth of experience and tried-and-true best practices, concepts and approaches will prove helpful in ensuring that patients will be meaningfully engaged in this data collection effort – but the right experts will have to be at the table when the data collection strategy for patient experience data is developed, implemented, and assessed.

For the reasons outlined above, NORD urges CMS to:

a. **Engage with CMS and FDA patient engagement experts and other relevant experts within CMS, HHS, as well as government-wide and within the private and non-profit sector.** This will help lay the foundation for a resilient and sustainable patient engagement system to rigorously engage patients and leverage the best practices and approaches to maximize the efficiency and chance of success.

We thank the Agency again for the opportunity to comment and look forward to working with CMS to ensure rare disease patients can fully participate in and benefit from the Negotiation Program.

Sincerely,

Heidi Ross, MPH
Vice President, Policy and Regulatory Affairs
National Organization for Rare Disorders

Karin Hoelzer, DVM, PhD
Director, Policy and Regulatory Affairs
National Organization for Rare Disorders

[7] https://bmchealthservres.biomedcentral.com/articles/10.1186/1472-6963-14-89
[8] https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment Instruments/QualityInitiativesGenInfo/Person-and-Family-Engagement

May 22, 2023

Submitted via
Electronic Filing: https://www.regulations.gov/document/CMS-2023-0043-0001

Centers for Medicare & Medicaid Services
Office of Strategic Operations and Regulatory Affairs
Division of Regulations Development
Attention: Document Identifier/OMB Control Number: CMS-10847, OMB 0938-NEW
Room C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

RE: Novo Nordisk Comments on *CMS-10847 Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act*

Dear Dr. Seshamani:

Novo Nordisk Inc. ("Novo Nordisk") appreciates the opportunity to provide comments in response to the information collection request ("ICR") issued by the Centers for Medicare & Medicaid Services ("CMS" or the "Agency"), entitled *Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act*.

Novo Nordisk is a global health care company committed to improving the lives of those living with serious chronic conditions, including hemophilia, growth disorders, diabetes, and obesity. The Novo Nordisk Foundation, our majority stakeholder, is among the top five largest charitable foundations in the world. Accordingly, our company's mission and actions reflect the Foundation's vision to contribute significantly to research and development that improves the lives of people and sustainability of society.

Novo Nordisk is a member of the Pharmaceutical Research and Manufacturers of America ("PhRMA"), and these comments incorporate by reference the comments submitted by PhRMA in response to CMS's ICR. In its comments, PhRMA notes, and Novo Nordisk emphasizes here, that some of the data sought by CMS in the ICR surpasses what is needed for the Agency to implement the Negotiation Program and conflicts with the requirement of the Paperwork Reduction Act to collect information in the "least burdensome" way possible. As discussed by PhRMA, the information CMS requests is vast in scope, imprecise, and in some cases duplicative. As a result, these requests impose a significant burden and raise serious concerns for manufacturers as to whether the ICR complies with the Paperwork Reduction Act. To assist CMS in properly

implementing the ICR and to promote an approach that best benefits patients, Novo Nordisk provides the following comments specific to certain aspects of the ICR.

In addition, Novo Nordisk has expressed concerns related to negotiation factors and data elements in comments we filed in response to the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (the "Guidance"). We will reference and reinforce some of our previous comments on the Guidance in this letter.

Finally, we believe that many aspects of the ICR are ultimately harmful to patients. Novo Nordisk is committed to improving the lives of patients and the sustainability of society. The ICR and the Negotiation Program more broadly serve to undercut the incentives of innovating that are essential to the sustained viability of pharmaceutical development. Setting prices based on concepts like whether a pharmaceutical manufacturer has recouped its research and development costs are poorly conceived and myopic. Novo Nordisk is concerned that longstanding innovative companies and start-ups alike will be disincentivized to undertake the monumental efforts of researching and developing new medicines if those risks are not properly rewarded. We fear patients ultimately will be harmed when fewer innovative treatments make it to market as innovators, researchers, and others decide that the risks are too great. We strongly urge CMS to implement this ICR by keeping front of mind the potential harm to patients that could come of this effort, and in recognition of the delicate balance that intellectual property laws have been designed to strike to stoke innovation.

CMS UNDERESTIMATES THE TIME AND BURDEN EXPENSES OF PREPARING AND SUBMITTING MANUFACTURER-SPECIFIC DATA

In Section B.12 of the Agency's Supporting Statement – Part A, CMS postulated a burden estimate of the time and resources it would take for Primary Manufacturers[1] to complete and submit the information requested on the Negotiation Data Elements ICR Form for the purpose of negotiation for a selected drug. Assuming that there will be ten Primary Manufacturers (one for each selected drug) for initial price applicability year 2026, CMS arrived at a conclusion of 500 total burden hours and $51,588.50 per manufacturer as a base estimate, with a low estimate of 250 hours and $25,794.25, and a high estimate of 1,000 hours and $103,177.00. We believe that these estimates are predicated on fundamental misunderstandings of the operations of a large and complex global pharmaceutical company like Novo Nordisk. Novo Nordisk has concerns that even the high estimate of the total burden hours and cost do not accurately reflect the time and resources necessary to provide the requested data elements to CMS.

[1] The term "Primary Manufacturer" is defined in CMS's Guidance. Certain terms referenced throughout these comments are consistent with CMS's definitions included in its Guidance.

In arriving at its burden estimates, CMS relied on inaccurate assumptions that skew the estimates lower than would be reasonably anticipated. For example, CMS referenced manufacturers' 10-K filings with the Securities and Exchange Commission, their reporting of Average Manufacturer Price under the Medicaid Drug Rebate Program, and certain state law reporting requirements. The Agency followed these scant examples with the broad conclusion that "Primary Manufacturers have experience providing information similar to the negotiation factors outlined in sections 1193(a)(4)(A) and 1194(e) of the Act." Supporting Statement – Part A, § B.12.

In truth, there is currently no authority under federal or state law that requires manufacturers to submit a large majority of the data elements in the form and manner specified by CMS in the ICR. CMS expanded the five manufacturer-specific data elements enumerated in section 1194(e)(1) of the Inflation Reduction Act ("IRA") into over thirty pages of vast yet imprecise definitions and instructions, imposing a slew of extra data gathering and submission requirements on manufacturers, many of which manufacturers have never before devised, determined, calculated, or produced. *See* ICR CMS-10847, OMB 0938-NEW §§ C–G. In many cases, these data do not exist in the ordinary course of business, particularly as they must be compiled in novel ways, such as at the 9-digit National Drug Code (NDC-9) or active moiety / active ingredient or mechanism of action levels.

An even bigger challenge is posed by data that may not exist at all, especially in relation to products that have been on the market for more than forty years. For example, in the case of Novo Nordisk, a company that has served the pharmaceutical market for over 100 years, there are significant challenges (if not impossibilities) of identifying with particularity research and development expenses associated with basic pre-clinical research that occurred over forty years ago, far predating existing financial and recordkeeping systems. Further still, Novo Nordisk is a global company with headquarters based outside the United States, meaning that information underlying many of the required data elements is spread across multiple individuals in various locations throughout the world. Novo Nordisk personnel in the United States would need to connect with global colleagues in other affiliates spanning various business functions to search for and access necessary information. Manufacturers will also need to complete important data validation checks, internal sign-offs, and related internal processes intended to help ensure that the data reported to CMS is accurate and complete, all of which require *substantial* time and resources. This effort is anticipated to far exceed the 30 days CMS has allotted.

CMS is also proposing that Primary Manufacturers would be required to collect and report certain data from Secondary Manufacturers. Among other material challenges and problems with that proposal described more below and in the comments we submitted on CMS's Guidance, Novo Nordisk is concerned about the extreme burden that such a requirement could put on Primary Manufacturers, especially because CMS does not offer any mechanism for how Primary Manufacturers should collect that information from Secondary Manufacturers.

Considering the novelty and breadth of the data requested in the ICR and the complications of obtaining and reporting data from Secondary Manufacturers – which is an unfair and potentially impossible task by itself, as described further below, it is difficult for Novo Nordisk to reasonably estimate what might be the time and burden on Primary Manufacturers in responding to the ICR. But we firmly believe that the assumptions on which CMS relied in establishing its burden estimates do not reflect the realities that manufacturers will face in preparing and submitting the data. CMS should revisit its burden estimates and thoughtfully consider the practical difficulties associated with the novelty of the ICR. We also respectfully request that CMS endeavor to decrease the burden on manufacturers, and our comments aim to suggest ways to meaningfully fulfill that goal.

CMS MUST AFFORD MANUFACTURERS MORE THAN 30 DAYS TO SUBMIT DATA

CMS also envisions that this information be collected and reported to the Agency within only 30 days. Providing the whole compilation of data requested will be a novel challenge for manufacturers within CMS's extremely limited 30-day timeframe. As noted above, even the high end of CMS's estimated time and burden estimate is likely to be grossly insufficient for Primary Manufacturers. Novo Nordisk believes that CMS has flexibility to implement the data submission timelines with respect to the manufacturer-specific data elements enumerated in section 1194(e)(1) and the evidence about alternative treatments detailed in section 1194(e)(2). CMS should afford manufacturers necessary and adequate time to prepare and submit data, and not implement a strict 30-day submission requirement. The Agency should permit manufacturers to make rolling data submissions, based on timelines that would be agreed to by CMS and each affected manufacturer. Such an approach would recognize the reality that there will be unavoidable circumstances in which more time is necessary to appropriately compile and provide accurate and complete data to the Agency.

MANUFACTURERS WILL BE REQUIRED TO MAKE MYRIAD REASONABLE ASSUMPTIONS IN PREPARING MANUFACTURER-SPECIFIC DATA, AND CMS MUST AFFORD MANUFACTURERS SUFFICIENT MEANS TO EXPLAIN THEIR ASSUMPTIONS

CMS must recognize and appreciate that manufacturers will need to make and rely on reasonable assumptions in providing much of the data to the Agency. Many of the requested data elements are new and novel, do not reflect how manufacturers prepare data for any other existing purposes, and are not maintained or devised in the ordinary course of business, particularly in the form and manner specified by CMS. For example, with respect to abandoned and failed drug costs, CMS stated that these costs "include a sum of the portion of direct *basic pre-clinical research* costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and a portion of direct *post-IND costs* for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval." *Id.* Novo Nordisk—likely along with many other manufacturers—does not delineate research and

development costs in these ways. The same is true for many of the other requested data elements. The need for assumptions will be greater in the absence of informed and detailed guidance from CMS that meaningfully addresses the decisions and related complications that manufacturers will face in compiling and providing this data. This is especially true in situations in which the data are difficult or impossible to obtain in the form requested by CMS. CMS must afford manufacturers reasonable discretion to make assumptions in preparing their data submissions and cannot impose civil monetary penalties in relation to data submissions that are based on reasonable assumptions, especially if the Agency does not provide clear and detailed guidance that would directly conflict with a manufacturer's reasonable assumption.

Novo Nordisk appreciates that CMS will offer manufacturers an opportunity to explain the manufacturer-specific data that they will provide. But we believe that the proposed word limits for many of the data elements will be insufficient to provide adequate explanation, especially considering the novelty of many of the data elements and the myriad assumptions that manufacturers will need to make. For example, as described in detail below, Novo Nordisk will need to make a series of critical assumptions in devising the unit costs of production and distribution for the selected drug, and we are concerned that the proposed limit of 2500 words will be insufficient. Accordingly, Novo Nordisk requests that CMS remove any word limit on the explanations that manufacturers will provide for each data element. Alternatively, CMS could use expanded word limits and also permit manufacturers to upload exhibits and related documents to further explain and clarify their reasonable assumptions.

PRIMARY MANUFACTURERS SHOULD NOT BE RESPONSIBLE FOR COLLECTING DATA FROM SECONDARY MANUFACTURERS, AND CMS'S PROPOSED RELATIONSHIP BETWEEN THE ENTITIES RAISES SIGNIFICANT CONCERNS

Both CMS's ICR and Guidance propose that Primary Manufacturers collect information described in section 1194(e)(1) from not only their own records but also collect and report much of this same information from Secondary Manufacturers. *See* Guidance § 50.1; ICR CMS-10847, OMB 0938-NEW § C. Primary Manufacturers that fail to do so within the specified timeframe "will be subject both to an excise tax under section 11003 of the IRA and a civil monetary penalty under section 1197 of the Act, the value of which will increase incrementally the longer the manufacturer is noncompliant." Supporting Statement – Part A, § B.6. CMS's Guidance notes that the civil monetary penalty would be $1,000,000 per day of violation. *See* Guidance § 100.2.

Yet, CMS ignores the enormous practical and/or legal problems that will result from requiring Primary Manufacturers to comply with these provisions vis-à-vis Secondary Manufacturers. CMS's guidance does not provide any mechanism for Primary Manufacturers to collect information from Secondary Manufacturers, and Primary Manufacturers cannot guarantee the accuracy or completeness of data from Secondary Manufacturers. Primary Manufacturers cannot ensure compliance with such requirements, unfairly putting them at risk of significant fines

and penalties; nor can CMS guarantee the confidentiality of the Secondary Manufacturers' proprietary information and data. Secondary Manufacturers who may be in contractual privity are still competitors (e.g., authorized generic manufacturers) and ordinarily sharing this type of information risks violating the antitrust laws.

CMS has previously recognized that forced sharing of data and information between competitors for price reporting purposes is not appropriate. *See* 81 Fed. Reg. 5267, 5266 (Feb. 1, 2016) ("We understand the [legal and logistical] challenges of obtaining pricing information from unrelated manufacturers. Therefore … we have decided to limit the line extension provision to provide that a drug by one manufacturer will not be treated as a line extension of a drug by a different manufacturer, unless there is a corporate relationship between the manufacturers. This will limit the obligation of manufacturers to collect pricing information from unrelated parties."). The same consideration should apply here, especially because nothing in the IRA supports CMS's proposed approach, as further discussed in Novo Nordisk's comments on CMS's Guidance. Accordingly, CMS should abandon its proposal to require Primary Manufacturers to collect and submit data from Secondary Manufacturers. The Agency should instead require that Secondary Manufacturers be responsible for submitting their data.

CMS MUST TAKE MEANINGFUL STEPS TO PROTECT THE CONFIDENTIALITY OF MANUFACTURER-SPECIFIC DATA

Section 1193(c) of the IRA provides that proprietary information (as determined by the Secretary) that a manufacturer submits "shall be used only by the Secretary or disclosed to and used by the Comptroller General of the United States for purposes of carrying out the [Negotiation Program]." CMS acknowledges that "proprietary information, including trade secret and confidential commercial or financial information, is protected from disclosure under Exemption 4 of the Freedom of Information Act (FOIA) (5 U.S.C. § 552(b)(4))." Guidance § 40.2.1. CMS also notes that it "intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of FOIA, and that strikes an appropriate balance between (1) protecting the highly sensitive information of manufacturers and ensuring that manufacturers submit the information CMS needs for the Negotiation Program, and (2) avoiding treating information that does not qualify for such protection as proprietary." For the initial price applicability year of 2026, CMS "intends to treat information on non-Federal average manufacturer price . . . as proprietary" and "intends to treat research and development costs and recoupment, unit costs of production and distribution, pending patent applications, and market data and revenue and sales volume data to be proprietary, unless the information that is provided to CMS is already publicly available, in which case it would be considered non-proprietary."

Novo Nordisk appreciates and agrees with CMS's plans to implement a confidentiality policy that is consistent with existing requirements (including Exemption 4 of FOIA) and CMS's

plans to treat as proprietary and confidential any information that is not already publicly available. But the ICR provides no details regarding how CMS intends to ensure that manufacturer-reported data remains confidential and would not be used for purposes not authorized by the IRA. Novo Nordisk requests that CMS provide additional details regarding its plans in this regard. For example, CMS should strictly limit access to the information to only those personnel who need to use it for purposes of the Negotiation Program, and require those personnel to sign strict non-disclosure agreements that include clear consequences for violations.

Novo Nordisk also strongly believes that CMS should afford manufacturers deference in making good faith determinations as to which specific data and information are proprietary and thus must be protected from public disclosure and subject to the protections around its use. Oftentimes only the manufacturer will be able to make reasonable determinations as to whether its data would be trade secrets or confidential commercial or financial information. CMS should treat as proprietary any non-public information that a manufacturer provides to CMS as a part of the negotiation process that the manufacturer designates as proprietary information.

Moreover, in the event that CMS would consider disclosing or using information that a manufacturer has designated confidential and proprietary, the Agency must provide manufacturers a reasonable opportunity to object to such disclosure or use, and to allow them sufficient time to take measures to prevent such unauthorized disclosure or use. That approach is consistent with Department of Health and Human Services regulations that govern FOIA requests (requiring that data submitters be provided 10 working days from the date of the FOIA request notice to object to disclosure of any part of the records), as well as FDA's practices in handling trade secret and confidential commercial information. *See* 45 C.F.R. § 5.42, 21 C.F.R. §§ 20.61, 314.430.

CMS'S REQUESTS RELATED TO MANUFACTURER-SPECIFIC DATA ELEMENTS ARE PROBLEMATIC AND POSE UNIQUE AND POTENTIALLY INSURMOUNTABLE CHALLENGES FOR MANUFACTURERS

Novo Nordisk is concerned that the manufacturer-specific data elements set forth in Appendix C of the Guidance and reiterated in the ICR (1) would in part impose new substantive requirements on manufacturers that exceed the scope of the authority granted by Congress (e.g., among other problems, CMS requests pricing metrics that are not set forth in the IRA and that have never before been established or devised); (2) cannot be implemented without notice-and-comment rulemaking because the IRA itself does not possess the requisite level of clarity to facilitate implementation of the manufacturer-specific data requirements through non-binding guidance; (3) would be misused by CMS for its own procurement purposes as a market participant and not for any regulatory reasons; and (4) would not be sufficiently protected from unauthorized use or disclosure beyond the negotiation program (as noted, CMS has not provided any details regarding its plans to protect this highly sensitive, proprietary information from unauthorized use or disclosure). Novo Nordisk also notes that many of CMS's definitions and instructions related

to the manufacturer-specific data elements pose their own unique problems and challenges, some of which may be insurmountable.

Research & Development Costs and Recoupment (Section C)

Section C of the ICR provides that CMS "is considering R&D costs to mean a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug falling into the categories" of (1) basic pre-clinical research costs; (2) post-Investigational New Drug (IND) application costs; (3) completed U.S. Food and Drug Administration (FDA)-required phase IV trials; (4) post-marketing trials; (5) abandoned and failed drug costs; and (6) all other R&D costs. *See* ICR CMS-10847, OMB 0938-NEW § C. CMS also notes that it is "calculating recoupment of R&D costs using the global, total lifetime net revenue for the selected drug." *Id.*

CMS provides a list of basic definitions and instructions to govern the gathering and reporting of these data but fails to consider the feasibility challenges that manufacturers may face in gathering this data. There are some data elements for which it could be difficult or impossible for manufacturers to determine based on the significant time that has passed since the research and development costs were incurred. Research for some products began decades ago. For example, researchers began studying multiple existing Novo Nordisk products in the 1980s. The records detailing the related costs associated with those efforts (including abandoned and failed drug costs) will be extremely difficult to identify -- even if the burden of doing so was justified. And even if the effort was undertaken, the information may in fact no longer exist in the company's documents or systems, especially considering the various system upgrades and changes that have occurred in the many years since those expenses were incurred. Even if some historic cost information would be accessible, that information is expected to be generalized in nature (e.g., data included annual reports, which is not itemized in any meaningful way that would be helpful here). Accordingly, in some cases, especially for products that have been on the market for many years, it would be incredibly difficult, if not impossible, to reasonably allocate a drug's research and development costs and the associated failed and abandoned drug costs. CMS instructs manufacturers "[i]f the length of the basic pre-clinical research period for the selected drug cannot be calculated, use 52 months ending the day before the first IND application went into effect." *Id.* This timeframe is arbitrary, lacks meaningful support, and does not accurately reflect the decades of work that manufacturers invest in the research and development of their products. Moreover, as noted, in many cases, the issue will not be whether the length of the basic pre-clinical research period for the selected drug can be calculated, but rather, based on the known research period, that there will be extreme difficulties producing data that cover such historical time periods. In those cases, to approach directionally accurate figures for these data elements that reflect the decades of work invested in the research and development of the products, Novo Nordisk would be required to rely on a series of assumptions and allocation methodologies. CMS must recognize and appreciate these hurdles, and understand that the data manufacturers will submit could be accordingly limited in its usefulness. Manufacturers also should not face the threat of fines or False Claims Act liability

based on good faith assumptions to provide the data requested, including in cases where there are substantial limitations in the data available.

CMS must also appreciate that there are a host of "Other R&D Costs" that manufacturers incur in developing and bringing products to market. These include, for example: costs associated with preparing IND, NDA, and BLA submissions, as well as IDEs, 501(k)s, and PMAs (for combination products); NDA and BLA submission user fees and program fees; costs associated with annual safety submissions (post approval); and costs associated with brand and non-proprietary naming and labeling assessments; among others. Moreover, manufacturers incur similar regulatory and development costs in other countries where they sell their products. CMS must not disregard these "other" costs or view them as less significant/material to the overall costs of developing products and bringing them to market.

Novo Nordisk also believes that it would be unfair of CMS to make a determination as to whether research and development costs have been recouped for a selected drug by considering/comparing a narrow set of research and development costs (generally, those associated with FDA-approved indications) against the global, total lifetime net revenue for the selected drug. Such a proposal fails to consider the reality of pharmaceutical product development and pricing, and would create an inaccurate false impression as to whether a manufacturer has actually recouped its costs to develop and bring a product to market. First, as noted, this approach ignores research and development costs that are unrelated to the FDA-approved indications, but that are nonetheless material costs that manufacturers incur in researching, developing and selling a product globally.

Second, the element of abandoned and failed drug costs mischaracterizes the process of pharmaceutical innovation at a large and diverse company like Novo Nordisk. CMS proposes to limit the data on abandoned and failed drug costs to those associated with the "same active moiety / active ingredient or mechanism of action" and "same therapeutic class." At Novo Nordisk, we believe that innovation requires risk, and failed efforts (even those that are unrelated to successful efforts) help pave the way to the development of critical medicines. We, like many of our peers, must consider our entire range of product development lines when pricing the relatively few products that are ultimately approved. The revenue we generate from our successful products must cover research and development (as well as other myriad costs) for our whole range of pursued research and development activities and initiatives. It is myopic and unfair to only consider the costs of research and development that are associated with the "same active moiety / active ingredient or mechanism of action" and "same therapeutic class" as the selected drug. Additionally, this proposal does not account for investments in generally applicable technologies or systems that benefit multiple research streams and platforms. As noted in the introduction to these comments, we fear that these shortsighted concepts will serve to undercut the incentives of innovating that are essential to the sustained viability of pharmaceutical development, all to the detriment of current and future patients.

Third, this proposed concept of focusing on recoupment of research and development costs would completely ignore other material global, lifetime costs that manufacturers incur in producing, distributing and selling their products, such as global, lifetime costs to produce and distribute their drugs and related global regulatory costs, among others. Those other costs would need to be considered as part of any attempt to determine whether a manufacturer has recouped its costs through revenue.

Accordingly, Novo Nordisk believes that there is a gross mismatch in the foundation of the costs versus revenue that CMS is currently proposing, which unfairly limits the actual costs incurred while construing broadly the revenue generated. As a threshold matter, Novo Nordisk strongly opposes the concept of considering whether research and development costs have been recouped for purposes of setting an MFP, as the IRA contemplates, because it is based on an inherent misunderstanding of the operations of a large and complex global pharmaceutical company like Novo Nordisk. CMS's limitations exacerbate our concerns that such an unfair concept also will be unfairly implemented. CMS proposes to truncate the true value of the actual costs invested in bringing successful pharmaceutical products to market. If CMS endeavors to make a determination as to whether costs have been recouped (despite the problems of and fallacies underlying such an attempt and our significant concerns about the feasibility and appropriateness of making that attempt), then CMS should at least consider lifetime, global costs that are associated with researching, developing, producing, distributing and selling the product, including related indirect costs, as well as comprehensive research and development costs associated with failures well beyond those associated with the "same active moiety / active ingredient or mechanism of action" and "same therapeutic class."

Current Unit Costs of Production and Distribution (Section D)

CMS proposes to define "costs of production" as "all (direct and allocation of indirect) costs related to: [p]urchase of raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals; [f]ormulation and preparation of the finished drug product; [q]uality control and testing of the drug; and [o]perating costs for personnel, facilities, transportation, importation (if any), and other expenses related to the preparation of the finished drug product for the selected drug." *Id.* § D. The Agency proposes to define "costs of distribution" as "all (direct and allocation of indirect) costs related to: [p]ackaging and packaging materials; [l]abeling; [s]hipping to any entity (e.g., distributor, wholesaler, retail or specialty pharmacy, physician office or hospital, etc.) that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer; and [o]perating costs for facilities, transportation, and other expenses related to packaging, labelling, and shipping to any entity that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer." *Id.* These data points would exclude both R&D costs and marketing costs. *Id.* Further, manufacturers must report the average unit costs of production and distribution for all of the NDC-9s included in the selected drug. *Id.* CMS proposes that

manufacturers report these unit costs for the 12-month period ending May 31, 2023 (for selected drugs for initial price applicability year).

Novo Nordisk does not maintain or devise a unit cost of production or distribution in the ordinary course of business in the manner that CMS proposes. For example, Novo Nordisk accounts for costs on a calendar year basis, and not on a May-to-May timeframe. In addition, there are numerous practical complications with developing these numbers, and we will need to make a host of critical assumptions on a range of questions, including, for example: How should the company standardize plant-to-plant production fluctuations? How should the company address batches scheduled to be produced outside the May-to-May timeframe? How can the company account for the cyclical nature of product demand when this timeframe fails to capture it? If the company must blend data from two calendar years to conform to CMS's timeframe, how can those assumptions be succinctly and reasonably explained to CMS?

This means that any unit costs or production and distribution reported to CMS likely will incorporate both actualized values and reasonable estimates. We want to impress upon CMS that the data manufacturers will submit for the unit costs of production and distribution will be based on myriad important assumptions. Manufacturers should not face the threat of fines or False Claims Act liability based on good faith assumptions to provide the data requested.

Prior Federal Financial Support (Section E)

CMS proposes to define the element of "Federal financial support for novel therapeutic discovery and development" as "tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and/or development related to the selected drug." ICR CMS-10847, OMB 0938-NEW § E. Further, "prior Federal financial support" is "Federal financial support for novel therapeutic discovery and development (as defined above) issued during the time period from when initial research began (as defined above in the R&D Costs subsection), or when the drug was acquired by the Primary Manufacturer, to the day through the date the most recent NDA/BLA was approved for the selected drug." *Id.* According to CMS, the Agency "may consider adjusting the preliminary price downward if funding for the discovery and development of the drug was received from Federal sources." Guidance § 60.3.4.

Novo Nordisk echoes PhRMA's concerns regarding CMS's approach to this data element, particularly as it relates to manufacturers' submission of the information. Like PhRMA, Novo Nordisk notes that CMS's proposed approach is needlessly duplicative and contrary to the fundamental goals of the Paperwork Reduction Act. Specifically, the Paperwork Reduction Act states that agencies must demonstrate that they have taken "every reasonable step to ensure that the proposed collection of information: . . . Is not duplicative of information otherwise accessible to the agency." 5 C.F.R. § 1320.5(d)(1). PhRMA notes, and Novo Nordisk emphasizes here, that for some data elements, CMS's ICR disregards this goal. Here, for example, as the conduits that

provide Federal funding to manufacturers, government agencies are already cognizant of the funds they expended to support pharmaceutical development. Manufacturers should not bear the burden of supplying to CMS information that is readily accessible to the Agency from these other sources, and CMS asking manufacturers to do so directly contradicts an enumerated purpose of the Paperwork Reduction Act.

Moreover, providing this information could pose a significant challenge for manufacturers, especially because the development of some pharmaceutical products began decades ago. As noted throughout these comments, manufacturers' financial and recordkeeping systems have evolved and turned over since Federal financial support may have first been granted. Manufacturers will be forced to operate within the bounds of this constraint, which may render some information inaccessible and therefore unreportable. In addition, for some of the information (e.g., research and development tax credits), many manufacturers will not retain documentation beyond the time necessary under applicable statute of limitations per Internal Revenue Service laws, which, in some cases and especially for older products, will mean that certain tax information is no longer maintained by manufacturers. Manufacturers should be permitted to conduct reasonable due diligence of their information and data to determine whether prior Federal financial support might have been provided that is within the scope of the reporting obligation. CMS should not impose fines or False Claims Act liability on manufacturers for their good faith due diligence, especially when CMS can otherwise obtain this information from the government bodies that provided the funding.

Further, as PhRMA notes, CMS intends to limit the research and development costs that manufacturers will report to FDA-approved indications of the selected drug, but the Agency's definition of prior support is not similarly tailored. If CMS intends to stay with its proposal to only consider research and development costs associated with the FDA-approved indications of the selected drug (despite our and others' objections), then CMS should be consistent by also considering only the support that is directly relevant to the labeled indications. CMS should also remove general tax credits that are not product-specific from the definition of "Federal financial support for novel therapeutic discovery and development."

Similarly, because pharmaceutical companies greatly contribute to the research and development process at large by funding academic scientists or collaborating with those in government-funded programs, CMS should limit its definition of "prior Federal financial support" to only that funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug. CMS should also only consider those patents and patent applications that are directly related to the selected drug.

Patents, Exclusivities, and Approvals (Section F)

The Agency's proposed guidance and instructions regarding patents, exclusivities, and approvals are ambiguous and problematic. For example, "CMS considers patents relevant to this data to include: [i] all pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired by the Primary Manufacturer relating to the selected drug as of September 1, 2023; [ii] patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product); and [iii] all patent applications, pending and approved, for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug in any form." ICR CMS-10847, OMB 0938-NEW § F (emphases added).

With respect to preparing and submitting the requested data, manufacturers will be limited by the vague terms of CMS's definitions and instructions. Yet manufacturers will be required to provide highly confidential and commercially sensitive information without assurance of adequate protection. And these disclosures directly impact adjustment of preliminary pricing. More clarity is required, for at least the following three reasons.

First, the Agency does not sufficiently explain the scope of what qualifies as patents "relating to" or "linked" to the selected drug. These phrases could be interpreted in several ways, each of which could have a unique effect on the Negotiation Program. This is particularly true given that the scope of Question 14 exceeds existing disclosure requirements for listing patents in the Orange and Purple Books. Question 14 includes a catch-all to "describe any patents included in the table above not listed in the FDA Orange Book or Purple Book but relate to the selected drug." This description requirement alone is unbounded in scope and any answer compels the manufacturer to divulge commercially sensitive information it would otherwise not provide—to anyone—in any other capacity.

Second, the requirement to identify all "pending" patent applications that could "reasonably be asserted" makes no sense because a manufacturer can only assert a patent that has been issued. CMS's definitions also would require the manufacturer to divulge work-product or mental impressions of attorneys about which patents a third party "could reasonably be" infringing. This, too, exceeds the bounds of any other existing requirement and cannot be justified here.

Third, we foresee challenges in gathering information regarding expired patents (Question 13), depending on the scope of that request and the amount of time that might have passed since the applicable patents expired. Expired patents should play no role in setting the price for any drug, so this burden far exceeds its benefit.

Even setting aside this lack of clarity regarding scope, the Agency also failed to describe how CMS intends to protect and maintain as confidential the information manufacturers submit

during the Negotiation Program. This is critically important here. Given the broad scope of patents and information falling within CMS's proposed definitions, manufacturers risk disclosure of highly confidential and commercially sensitive information to their competitors. For example, CMS indicated in its Guidance that it "intends to treat . . . pending patent applications . . . [as] proprietary, unless the information that is provided to CMS is already publicly available, in which case it would be considered non-proprietary." Guidance § 40.2.1 (emphasis added). Novo Nordisk appreciates CMS's intentions with respect to pending patent applications but emphasizes that there are similar sensitivities around approved patents, especially those that are not required to be listed in the Orange Book or Purple Book and not otherwise publicly known as being associated with a selected drug. Manufacturers must be permitted to make good faith determinations as to which patent information included in their data submissions is confidential proprietary information, including commercially sensitive information that CMS must protect from disclosure. CMS must recognize and appreciate that such designations are not limited to only pending patent applications.

Regarding price-setting, CMS turned the financial incentive to obtain patents upside-down. Section 60.3.4 of the Guidance states that CMS "intends to consider the length of the available patents and exclusivities before the selected drug may no longer be single source. For example, if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward." (emphasis added). This is the opposite effect that manufacturers would anticipate -- and that Congress intended, as a means to incentivize innovation -- valid and enforceable patents to have on price.

It is shortsighted and unfair for CMS to penalize manufacturers whose drugs have ongoing patents and exclusivities. Patents were contemplated by the U.S. Constitution, and they incentivize continued research and development, particularly in the pharmaceutical industry. Manufacturers should not be penalized or discouraged from pursuing patents and exclusivities for their intellectual property, and CMS adjusting the preliminary price downward based on these efforts seeks to undermine both necessary innovation and well-established intellectual property law and principles. Novo Nordisk respectfully requests that CMS reverse its thinking and consider adjusting the preliminary price upward if the selected drug has patents and exclusivities that will last for a number of years.

Market Data, Revenue, and Sales Volume Data (Section G)

CMS outlines a host of price points and metrics that manufacturers would be required to calculate and submit under the purported rationale that these data would be "market data and revenue and sales volume data for the drug in the United States." CMS's proposed metrics include the following six distinct price points that are not defined by the IRA or any other law, and that are not otherwise required to be devised or reported by manufacturers: (1) "U.S. commercial average net unit price" (question 31); (2) "U.S. commercial average net unit price─ without patient assistance program" (question 31); (3) "U.S. commercial average net unit price─ best" (question

31); (4) "Manufacturer average net unit price to Part D Plan sponsors" (question 33); (5) "Manufacturer average net unit price to Part D Plan sponsors─ without patient assistance program" (question 33); and (6) "Manufacturer average net unit price to Part D Plan sponsors─ best" (question 33).

Novo Nordisk strongly opposes CMS's proposal to require manufacturers to report these six novel price points. Among other problems, the ICR does not provide nearly enough guidance on how to calculate and ascertain these novel price points. The instruction that CMS does provide in the ICR fails to explain these calculations with sufficient clarity to permit manufacturers' effective and accurate reporting. CMS is uniquely aware of the complexities and difficulties attendant to asking a manufacturer to translate commercial transactions into reportable drug pricing metrics. There are literally hundreds of pages of statute, regulations, FAQs, guidance, and related information published by the government over the last thirty years on how manufacturers should calculate and report established pricing metrics like Average Manufacturer Price, Best Price, 340B ceiling price, and Average Sales Price. Yet CMS purports to create and enforce six entirely new pricing metrics in less than six months and just a few pages of guidance.

These price points raise dozens if not scores of substantial questions about how they are to be calculated and reported. As CMS knows, there are myriad critical decisions and interpretations that manufacturers will need to make to fill in the gaps of these new proposed metrics, including, for example: how sales should be determined; how discounts, rebates, chargebacks, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered to any purchasers should be treated and allocated across NDC-9s and quarters; how coupons and co-payment assistance to patients should be treated and allocated across NDC-9s and quarters; among many other questions and decision points. We anticipate that there would be dozens or more questions and decisions that would arise when manufacturers actually started to perform these calculations. Manufacturers appreciate that CMS will need information on which to base MFP offers, but CMS cannot simply throw out slightly articulated, never-before-imagined metrics purporting to reflect an exceedingly dynamic and complex industry and expect compliant, consistent, useable information in return. Accordingly, Novo Nordisk believes that it would be impractical and infeasible to require manufacturers to develop and report such new and novel price points, and that CMS should remove these new price points from any manufacturer-specific data requirements.

In addition, CMS specifically asks for feedback on whether the 340B ceiling price (questions 21 & 22) and 340B prime vendor program price (questions 23 & 24) should be included in the required manufacturer-specific data elements. Novo Nordisk believes that these price points should have no bearing on CMS's determination of an MFP and that they are not necessary, relevant, or useful to the operation of the Program. Statutorily-mandated government discounts, including 340B pricing, are not a reasonable basis on which to build a "fair" commercial price of any kind. Manufacturers should not be required to provide this information as part of

manufacturer-specific data and CMS should not otherwise consider these metrics for purposes of the Negotiation Program.

Finally, for many of the other metrics in Section G—better known than the six new metrics discussed above but nonetheless rife with uncertainty—CMS does not provide adequate instructions to enable consistent approaches across manufacturers. The following includes a list of preliminary questions, concerns, and related feedback from Novo Nordisk on the metrics noted.

- WAC Unit Price (questions 19 & 20): CMS asks for the WAC unit price for each applicable NDC-9 and the total number of units sold to wholesalers and direct purchasers during each quarter for the most recent five years, as applicable. There are a number of questions and decision points that CMS will need to resolve, including, for example: Should WAC be reported as of the first day or last day of each quarter, or should manufacturers report the average WAC over each applicable quarter? If an average should be used, should it be a weighted average? There are also complications that arise when a common NDC-9 actually has different per-unit WACs due to different package presentations. In those cases, which WAC should be reported for the NDC-9? In addition, manufacturers will need additional details regarding how to determine and report the unit volume sold by quarter, including, for example: Should returns be considered?

- Best Price (questions 25 and 26): CMS asks for Medicaid best price information as was submitted under the Medicaid Drug Rebate Program ("MDRP"), including any restatements that have been certified under the MDRP, as well as the total unit volume for the quarter, reflected as the sum of monthly average manufacturer price ("AMP") units reported to the MDRP for the quarter. Manufacturers will be required to report this information for each quarter during the most recent five years, as applicable. In the event that a manufacturer updates and recertifies its best price for a particular quarter after it submits its manufacturer-specific data to CMS, would the manufacturer be expected to update the data it previously submitted to CMS?

- Federal Supply Schedule ("FSS") Price (questions 27 and 28): CMS asks for FSS price as reflected online in the Pharmaceutical pricing data for all VA National Acquisition Center ("VA NAC") programs, as well as the total number of units for each NDC-11 sold to direct federal purchasers, for each applicable price period for the most recent five years. Novo Nordisk has a number of questions regarding what specifically should be reported. First, we presume that the FSS price reported should reflect published national contract prices as set forth in VA NAC data as "FSS Price." We also presume that this metric should not reflect prices for the Big Four, which would be reflected in the data element for the "Big Four Price." To help improve consistency in approaches between and among manufacturers on this data element, Novo Nordisk requests that

CMS specify which particular price should be pulled from the VA NAC program pricing database.

- Big Four Price (questions 29 and 30): CMS asks for the Big Four price as reflected online in the Pharmaceutical pricing data for all VA NAC programs, as well as the total number of units for each NDC-11 sold to the Big Four federal agencies (Department of Veterans Affairs, Department of Defense, the Public Health Service, and the Coast Guard), for each applicable price period for the most recent five years. Because the Big Four Price is also an FSS price, Novo Nordisk asks that CMS provide more specificity between what is required for this data element as compared to the separate request relating to the FSS price. For example, we presume that manufacturers should specifically report the Big Four Prices as published on the VA NAC program pricing database as the "Big 4 Price."

Evidence About Alternative Treatments (Section H)

Novo Nordisk reiterates the concerns PhRMA raises in its comments related to CMS's proposed approach to collecting "Evidence About Alternative Treatments," and similarly supports the suggestion that CMS minimize burden on manufacturers by both allowing for the rolling submission of data and identifying the therapeutic alternative(s) they will consider at the time the list of selected drugs is published. Taken together, this will allow manufacturers to better focus the information provided and avoid submitting, for example, comparative clinical effectiveness information involving treatment alternatives not in scope. This is significant particularly because there is likely to be a large volume of clinical and real-world evidence for products approved at least seven or eleven years ago across all indications and forms.

Like PhRMA, Novo Nordisk sees little utility in CMS asking respondents, as it does in Questions 40-43: "Does any evidence provided treat extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled or not terminally ill?" As worded, and without clear standards about what might constitute treating extending the life of certain populations "as of lower value" than others, this question is unlikely to provide CMS with reliable information to ensure it meets its statutory obligation not to consider such evidence outlined in section 1182(e)(2). Accordingly, we suggest it be deleted.

Novo Nordisk also believes that additional clarification is needed for the terms "therapeutic advance" (Question 41) and "unmet medical need" (Question 43). Neither the instructions for questions in Section H nor Section 60.3.3.1 of the Guidance adequately explain what CMS will consider to be "improvements in outcomes compared to [a selected drug's] therapeutic alternative(s)." Additionally, CMS's definition of "unmet medical need" as provided in the Guidance and the Instructions for Question 43 is overly narrow and thus inadequate, especially when applied to complex medical conditions. At the very least, CMS should adapt its definition to

align with the FDA's definition, which considers other dimensions beyond the number of treatments available such as improved compliance, reduced toxicity, and improved tolerability.

* * * *

Thank you for considering Novo Nordisk's comments. We would be pleased to discuss these comments with you in further detail. If you have questions, please contact Jennifer Duck, VP, Public Affairs at JEDK@novonordisk.com.

Filed electronically via federal eRulemaking Portal: http://www.regulations.gov

Mr. William N. Parham, III
Director, Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
U.S. Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Inflation Reduction Act (IRA) Drug Price Negotiation Data Elements Information Collection Request (CMS-10847)

Dear Mr. Parham:

On March 21, 2023, the Centers for Medicare & Medicaid Services (CMS) announced in the *Federal Register*[1] an Information Collection Request (ICR) Form, as required by the Paperwork Reduction Act (PRA), for Negotiation Data Elements[2] under Sections 11001 and 11002 of the Inflation Reduction Act (IRA). This ICR follows the guidance published by CMS on March 15, 2023 in which it describes the process by which it will initiate negotiations with drug manufacturers for selected drugs, among other topics.[3]

PCMA is the national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans and operate specialty pharmacies for more than 275 million Americans with health coverage through Fortune 500 companies, health insurers, labor unions, Medicare, Medicaid, the Federal Employees Health Benefits Program, and plans offered for sale on the Exchanges established by the Affordable Care Act. PBMs negotiate price concessions with manufacturers on their brand medications to improve the value of the Part D program. These price concessions reduce premiums for all beneficiaries and provide access to preferred drugs with reduced cost sharing. Negotiated drugs under the IRA will be priced no higher than the prices PBMs are already able to negotiate. We have an interest in ensuring that manufacturers do not find loopholes in the CMS program, so that Part D plans and their contracted PBMs have certainty as we continue to negotiate on behalf of the program for drugs not selected by CMS.

Per the guidance, CMS will require manufacturers of selected drugs to submit a specified list of data elements. CMS states that it intends to develop an automated tool within an existing information technology system, the Health Plan Management System (HPMS), for Primary Manufacturers and the public to report these data. CMS is also proposing to require any individual or entity submitting data for purposes of the Drug Negotiation Program to submit an attestation regarding the accuracy and completeness of the data submitted.

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[1] 88 FR 16983
[2] CMS-10847. Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act. March 21, 2023
[3] Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments (cms.gov)

Pharmaceutical Care Management Association
325 7th Street, NW, 9th Floor
Washington, DC 20004
www.pcmanet.org

Overall Comment: CMS Should Validate Manufacturer-Submitted Data Against Public Sources

In general, many of the CMS requested elements are publicly available. Relying on manufacturer submissions on a timely basis may lead to unnecessary delays in CMS's work. We strongly encourage CMS to consider acquiring as much of these data as it can, on its own, from other government agencies. We acknowledge that CMS may need to enter into data use agreements or memoranda of understanding with other agencies, but the upfront time commitment to doing so will expedite future years' work and allow CMS to more efficiently determine appropriate maximum fair prices (MFP).

An Overview of Formulary Construction and Price Negotiation Today

Part D plan sponsors rely on PBM expertise to secure savings through price concessions from drug companies, to partner with lower cost, higher quality pharmacies, and to address clinical areas like medication adherence. When assessing a new drug for coverage, developing a formulary *de novo*, a plan's Pharmacy and Therapeutics (P&T) Committee evaluates therapeutic alternatives, the novelty of the drug in terms of meeting an unmet medical need. Upon deciding whether to include a drug on the formulary, the PBM then negotiates with the drug's manufacturer for tier placement and utilization management, in line with the P&T Committee's recommendations. These negotiations can include rebates and other price concessions. The result is a formulary that is both clinically appropriate and aligned with the plan's interests in the lowest net cost.

Discussion of Data Elements to be Submitted by Manufacturers of Selected Drugs

The ICR lists a range of data elements and sub-elements for which CMS has been instructed to collect data from manufacturers when considering the initial pricing offer. In general, CMS will be collecting more data than is needed to make an informed offer. Many of these data elements do not enter into the decision-making by P&T committees, PBMs, and plan sponsors, for example. Our intent in providing comments is to highlight where the data CMS will receive will be of high value compared to low value in determining the right initial offer price. We respond to each major category of data elements in Table 1 and highlight select sub-elements in our responses.

Table 1: PCMA Commentary on Specific Data Elements Sought by CMS

ICR Data Elements	PCMA Commentary
Research and development (R&D) costs of the Primary Manufacturer for the selected drug and extent to which the Primary Manufacturer has recouped R&D costs.	From PCMA's perspective, the work of P&T committees does not consider R&D costs during drug evaluation for inclusion in formularies and for tiering and prior authorization determination processes. Given that many products and failed attempts at drug development can be assessed as R&D costs, these data points should not be the focus of data collection unless CMS creates a weighting scheme based on total amount of R&D costs and the amount of unrecouped R&D costs. Focusing negotiations on R&D costs would dictate terms to the market and signal to manufacturers how to influence the negotiations going forward.

ICR Data Elements	PCMA Commentary
Manufacturer-Specific Data	As CMS is aware, the U.S. Food and Drug Administration (FDA) controls the master list of the 11-digit NDCs. Therefore, even though manufacturers must self-identify all applicable labeler and product codes, CMS can and should validate this data against FDA's database, and other federal agency records regarding ownership status. Since CMS will define qualifying single source drug (QSSD) very broadly (combining all dosage forms and strengths into the same drug product), it should be aware that P&T committees often look at these in different ways. Some forms are more effective for certain uses, have different competitors, or pose different safety risks. The negotiation with the manufacturer may treat each form of the drug differently. As CMS is also aware, non-Federal Average Manufacturer's price (NFAMP) is a pricing benchmark. Manufacturers are required to establish Federal Ceiling Prices (FCP) for new covered drugs that are introduced to the commercial marketplace. In order to establish an FCP, manufacturers are required to submit a report that contains NFAMP report to PBMs. Requiring manufacturers to submit these data to CMS through the HPMS system, rather than CMS acquiring them directly from PBMs may be cumbersome and result in incomplete data.
Current unit costs of production and distribution of the selected drug	The supply chain is vast and complex, and we are concerned that manufacturers will try to tar other participants who are behaving within expected parameters when providing these data. For example, manufacturers sell to wholesalers or specialty distributors. Pharmacies (retail, mail order, and specialty), hospitals, physician offices, and other facilities may purchase them through these channels. The pricing for each entity is negotiated between the seller and the purchaser. Additional discounts from manufacturers can be negotiated as well. CMS would be bogged down in data that does not drive manufacturer pricing decisions if it accounts for these facets. PBMs may, however, account for the complicated nature of channel delivery and patient access for specialty drugs, as part of their considerations on whether it should be available through specialty pharmacies, but not in terms of coverage or pricing, directly.
Prior federal financial support for novel therapeutic discovery and development with respect to the selected drug	We agree that manufacturers should volunteer this information. This is relevant especially as it pertains to federal health care program purchases. However, CMS should also enter into collaborative agreements with National Institutes of Health (NIH), Administration for Strategic Preparedness and Response (ASPR)- Biomedical

ICR Data Elements	PCMA Commentary
	Advanced Research and Development Authority (BARDA), Defense Advanced Research Projects Agency (DARPA), and other federal research organizations to collect this information for validation purposes. This information is not typically considered during PBM P&T Committee's drug inclusion deliberations.
Data on pending and approved patent applications	This information is not considered during PBM P&T Committee's drug inclusion deliberations. This information is future focused and would not be used as a determinant for potential cost and pricing for drugs. PBMs, instead, monitor these patent expiration and loss of market exclusivity dates in anticipation of increased price competition.
Data on exclusivities recognized by the Food and Drug Administration (FDA)	CMS should consider if there is value in requiring that drugs with extended exclusivities should have lower MFPs than those that do not. This information is only helpful if there is a direct correlation between longer exclusivities and higher prices. PBMs and P&T committees will consider drug indications and exclusivities during their deliberations, as noted above.
Data on applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act	505(c) information may not be available to the specified manufacturer but is available through FDA. CMS should work with FDA to understand the status of submitted generic drug applications and User Fee dates and likely approval timelines. The IRA clearly combines any spending for authorized generics into the QSSD under the primary manufacturer or any secondary manufacturers.
Market data and revenue and sales volume data for the selected drug	Aside from Quarterly Total U.S. Gross and Net Revenue, Quarterly Total U.S. Unit Volume, and commercial net price, CMS can get all of these from other government agencies (or from itself) for purposes of this program. While having the manufacturer submit might save CMS a step, these data need to be validated against actual government records. Please note that CMS may be setting itself up for additional time reconciling data if manufacturers dispute how CMS or the relevant federal agency aggregates their data.
Therapeutic Alternative Data	PBM P&T committees consider therapeutic alternatives and all drug indications when making their coverage decisions. This consideration addresses availability of "me too" similar drugs. CMS needs to consider whether drugs with a lot of lower price alternatives should have lower MFP whereas drugs with fewer or only higher priced alternatives would have an MFP closer to the ceiling price.

Conclusion

We hope CMS appreciates the discussion in this letter, from an interested industry stakeholder, as it looks to finalize key details of the Negotiation Program. It is critical to the PBM industry that data submitted by manufacturers to CMS be meaningful and interpreted and used in a way that

helps achieve CMS's aims. Our belief regarding validation through existing sources – or replacing these outright with external data – is that if manufacturers are providing fewer data elements, there are fewer data elements that they can use to argue for a higher MFP. We hope our suggestions help CMS finalize data elements to be collected from manufacturers. If you have any questions on these suggestions and recommendations, please do not hesitate to contact me directly at tdube@pcmanet.org.

Sincerely,

Tim Dube

Tim Dube
Vice President, Regulatory Affairs

950 F STREET, NW, SUITE 300 • WASHINGTON, DC 20004 • 202-835-3400 • PhRMA.org

APPENDIX A.

April 14, 2023

VIA Electronic Filing – *IRARebateandNegotiation@cms.hhs.gov*

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attn: PO Box 8016

Re: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

Dear Deputy Administrator Seshamani:

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to respond to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance) which was released by CMS on March 15th, 2023.[1] PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested more than $1.1 trillion in the search for new treatments and cures, including $102.3 billion in 2021 alone.

While PhRMA is pleased to comment on portions of the Guidance, we also have significant concerns about the content of the Guidance, as well as the policies the Guidance implements. The drug pricing provisions of the Inflation Reduction Act (IRA) establish an unprecedented new price-setting authority for medicines in Medicare. This represents a seismic shift from the current market-based systems that underpin both Medicare Part D, which relies on competing plans to control costs, and Medicare Part B, which pays for physician-administered medicines based on discounts available in the market. PhRMA is deeply concerned that this shift will erode patient access and undermine continued biopharmaceutical innovation, particularly progress that occurs after a medicine's initial approval by the U.S. Food and Drug Administration (FDA).

Unfortunately, the Guidance only serves to reinforce and increase our concerns. What the drug pricing provisions of the IRA require is not "negotiation." Unlike negotiations manufacturers enter into with health plans, the Secretary will set prices for selected drugs and enforce them with the threat of legal penalties so severe that no manufacturer could afford to incur them. Given these dynamics, it is imperative that the Guidance establish clear

[1] Available at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf

standards and processes to assure stakeholders that CMS' decision making will not be arbitrary and can be influenced by data presented by manufacturers. Unfortunately, the Guidance fails this test. Instead, the Guidance would allow CMS to consider virtually any evidence, and assert that its review of the evidence supports any virtually any decision without any recourse to hold CMS accountable for not following a "consistent methodology", as required by statute.

Indeed, the Guidance describes an approach that fails to give manufacturers and public stakeholders sufficient predictability and transparency. In particular, PhRMA is concerned that the Guidance:

- Provides inadequate (in some cases non-existent) opportunities for meaningful input on the Guidance, as well as the manufacturer "Agreement";
- Establishes requirements as part of the manufacturer Agreement that would undermine the effective implementation of the "Medicare Drug Price Negotiation Program" (the Program), including onerous prohibitions against manufacturers disclosing any information about their experiences under the Program;
- Fails to define a methodology and process for setting "Maximum Fair Prices" (MFP) that are consistent, objective, and predictable; and
- Appears to suggest an approach to determining MFPs that explicitly penalizes innovation.

Specifically, the Guidance implies that CMS is planning to use its discretion to set MFPs using a "cost plus" approach. Suggestions of this approach in the Guidance include statements that CMS "may" use factors such as research and development costs, production and distribution costs, and remaining patents and exclusivities to reduce the price the Secretary would otherwise set for a drug based on the clinical benefits it offers to patients. This approach is wholly incompatible with the economics of the research-based biopharmaceutical sector, in which returns on a small share of commercially successful medicines set investment incentives.[2,3] Such an approach also devalues therapeutic performance, would be exceptionally destructive to the development of new medicines and indications, and is unnecessary to achieving savings under the law. CMS cites its latitude to determine how or to what degree each factor should be considered. Rather, it should use that latitude to fairly assess the clinical benefit of selected drugs offered to patients and decisively reject a "cost plus" approach.

Compounding problems, the Guidance also falls short of legal requirements, as well as what is widely acknowledged to be a sound policy development process, allowing only 30 days of comment for a program CMS acknowledges is "novel" and "complex."[4] CMS is incorrect that the Guidance is exempt from procedural requirements of the Medicare statute or the Administrative Procedure Act (APA) and that the Agency need only "voluntarily" accept comments. Under the APA, the Guidance is a legislative rule; under section 1871 of the Social Security Act (SSA), program guidance or program instructions that establish a "substantive legal standard" must be issued with notice and 60 days of comment in the *Federal Register*.[5] CMS also is wrong to rely on the statutory deadline of September 1st, 2023 as "good cause" to waive notice and comment. CMS waited until

[2] CBO. (2021). Research and Development in the Pharmaceutical Industry. Available at: https://www.cbo.gov/publication/57126.
[3] See DiMasi JA, Grabowski HG, Hansen RW, "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," Journal of Health Economics, vol. 47 (May 2016), p. 25, https://doi.org/10.1016/j.jhealeco.2016.01.012.
[4] 87 Fed. Reg. 62433 (Oct. 14, 2022).
[5] *Azar v. Allina Health Services*, 139 S. Ct. 1804 (2019). *See also* HHS Office of the General Counsel, Advisory Opinion 20-05 on Implementing *Allina* (Dec. 3, 2020), https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/2101111604-mh-advisory-opinion-20-05-on-implementing-allina_12.03.2020_signed.pdf. CMS cites to Congress' direction to implement through program instruction or other forms of guidance, but such direction does not explicitly supersede section 1871 or APA requirements. The provision requiring program guidance is not prefaced with a "notwithstanding" clause, a phrasing that would have clarified the IRA's preemptive intent. "Repeals by implication are not favored, and are a rarity." *Maine Cmty. Health Options v. United States*, 140 S. Ct. 1308, 1323 (2020) (cleaned up).

March (approximately seven months after IRA enactment) to publish the Guidance; the fact that the Agency waited longer than it should have to publish guidance does not exempt it from providing required opportunities for stakeholder comment.

We are particularly troubled that the Agency chose to publish a critically important aspect of the Program – "Identification of Selected Drugs for Initial Price Applicability Year 2026" (section 30) – as final, without opportunity for any public input or comment.[6] The issues addressed in section 30 are extremely important to patients including which drugs and forms would be subject to price setting, the statute's orphan drug exclusion, and the biosimilars pause. It is a grave error for CMS to adopt the approach outlined in that section without giving stakeholders an opportunity to comment. Manufacturers and PhRMA have expertise in these area and are uniquely positioned to provide CMS with the type of feedback needed on foundational decisions such as the definition of a "qualifying single source drug" (QSSD)and the biosimilar pause. Providers, pharmacies, patients, and their caregivers also provide perspectives CMS should consider in a novel and complex program that sets prices and new reimbursement rates for medicines in Medicare. Finalizing section 30 without notice and comment denies the Agency the expertise of all stakeholders and raises serious legal questions under section 1871 of the SSA and the Due Process Clause of the U.S. Constitution. The approach outlined in section 30 will have far-reaching consequences for PhRMA members and for patients. Most critically, it will shape how innovative biopharmaceutical companies allocate scarce resources as they develop the next generation of treatments and cures, which will be used by patients both inside and outside of the Medicare program. PhRMA notes CMS' statement that it "may make changes to any policies, including policies on which CMS has not expressly solicited comment, based on the Agency's further consideration of the relevant issues." We urge the Agency to reconsider this position and engage on these important matters in the future.

Despite these significant concerns with the Guidance, PhRMA recognizes that CMS has a statutory obligation to implement the Program. Our comments outline recommendations the Guidance can mitigate the harm to patient access and innovation over time. Below we summarize those recommendations for CMS.

REQUIREMENTS FOR MANUFACTURERS OF SELECTED DRUGS (Section 40)

- Abandon the Primary/Secondary manufacturer definition and instead enter into separate Agreements with each manufacturer, as anticipated by the statute.
- Allow manufacturers enough time to comment on the Agreement language before the Agreement deadline; avoid use of open-ended language in the Agreement.
- Open the "confidentiality policy" for public comment and ensure the policy and protocols offer robust protection and security of proprietary information, as outlined in comments below. Abandon the proposed data use limitation as it violates the First Amendment, conflicts with government transparency principles, and cannot be finalized.
- Establish a process to effectuate the MFP for eligible patients that provides manufacturers with access to needed data from the Part D Prescription Drug Event (PDE) records in order to verify that the patient is an MFP-eligible individual.
- Work in coordination with the Health Resources and Services Administration (HRSA) to revise the Guidance to prevent duplicated MFP and 340B discounts as required under the IRA.

[6] There is an extremely narrow exception for the Small Biotech Exception Information Collection Request (ICR).

NEGOTIATION FACTORS (Section 50)

- Use – and allow manufacturers to submit data from – the FDA's Orange and Purple Book listings and Drugs@FDA for relevant patent information.
- Allow manufacturers to voluntarily provide additional data, as manufacturers need discretion due to the varied ways in which they record and maintain data on these factors.
- Amend the Information Collection Request (ICR) guidance to allow manufacturers to note where they have provided requested data and ensure that there is sufficient space for companies to provide rationale and references for approximate data calculations.
- Place minimal weight on recoupment of research and development (R&D) costs, and specify that this factor will not be used to reduce an MFP; count only a fraction of global net revenue toward "recoupment" of R&D costs.
- Amend the Guidance to limit required submission of R&D costs to data available to the manufacturer that can be directly attributable to the selected drug, while allowing companies to voluntarily provide supplemental data and a supportive narrative.
- Allow manufacturers to rely on benchmark or industry-wide data in cases where a company may not maintain the data.
- Remove the tax credits from the definition of "prior federal financial support" and limit consideration to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug (e.g., excluding basic science, research tools, or similar general concepts).
- Reverse the proposal that penalizes manufacturers for having patents and exclusivities by instead increasing the preliminary price to reflect the innovation in the product.
- Explicitly acknowledge statutory prohibitions against the use of quality-adjusted life years (QALYs) and similar metrics, in any context based on both the language in the IRA and the SSA.
- Require that entities attest to removing all QALY-based research from their data submissions to CMS, including research where the findings were intrinsically influenced by the use of QALYs.
- Develop robust literature review and research standards for the Agency and all external organizations CMS works with on evidence synthesis and technology assessment, both formally and informally, to ensure that the evidence it relies upon or develops is methodologically rigorous and patient-centered.

NEGOTIATION PROCESS (Section 60)

- Set MFPs for selected drugs at or near the ceiling price for all Medicare Part B and Part D medicines beginning with the first several "initial price applicability years" (IPAY) in view of the short timeline for implementation and novelty of the Program.
- In subsequent years, consider setting the MFP for "selected drugs" at the ceiling price in the following circumstances:
    - Selected drugs for which the IPAY is less than 13 years since the medicine's initial FDA approval, to mitigate consequences of the Program for small molecule medicines;

- Selected drugs for which the statutory ceiling price is the net price, reflecting significant discounts through brand-to-brand competition;
- Selected drugs that meet or have met the FDA's definition of unmet need, evaluated across a product's lifecycle;
- Selected drugs that meet or have met the New Technology Add-On Payment's (NTAP) definition of "substantial clinical improvement", and therefore represent a significant therapeutic advance; and
- Any selected oncology drug that receives a Category 1 or 2A rating in the National Comprehensive Cancer Network's Drugs and Biologics Compendium, and therefore represents a significant therapeutic advance.

- Prior to making its initial offer to the manufacturer, CMS should publish and solicit public comment on key elements of its MFP analysis including, but not limited to: 1) therapeutic alternative(s) CMS has identified for any selected drug it is considering (for each indication); 2) data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 3) benefits and impacts of a selected drug CMS intends to consider; and 4) stakeholders, and other government agencies and organizations CMS intends to engage, formally or informally.
- Place a greater weight on the factors related to the benefits that medicines actually offer to patients, caregivers, and society as specified in section 1194(e)(2).
- Engage relevant experts – including manufacturers and clinicians – as the primary resources for determining therapeutic alternative(s) and provide an opportunity for feedback on therapeutic alternative(s) before the initial offer is made.
- Use "clinically appropriate" as the standard for decision-making as to a selected drug's therapeutic alternative or comparator; do not rely on cost to select "therapeutic alternative(s)" and comparators.
- Consider a comprehensive range of clinical and non-clinical benefits and impacts of a selected drug, including those that are important to patients, caregivers, and society, based on feedback from those stakeholders. Include in the explanation a detailed account of how CMS identified relevant benefits and impacts of a selected drug, data and analysis on each benefit and impact for the selected drug, and how each contributed to the selected drug's MFP.
- Provide manufacturers of selected drugs the opportunity to meet with Agency staff at least three times in-person prior to the manufacturer's counteroffer: 1) after drug selection but prior to initiation of the price-setting process; 2) prior to CMS presenting the initial offer; and 3) after CMS presents the initial offer.
- Use the annual non-Federal average manufacturer price (non-FAMP) already in use by the U.S. Department of Veterans Affairs (VA), as defined in 38 U.S.C. § 8126(h)(5), in MFP calculations.
- Describe the template that will be used for the initial, concise justification and ensure it includes: 1) how therapeutic alternative(s) for each indication were selected; 2) how each factor was weighed; 3) data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 4) benefits and impacts considered; and 5) stakeholders, and other government agencies and organizations CMS engaged, formally or informally, in the process and how their input factored into the Agency's offer.
- Publish the required IPAY 2026 explanation for the MFP before the IPAY 2027 price setting process begins and ensure that all explanations include, at a minimum: 1) therapeutic alternative(s) for each indication and how they were selected; 2) how each factor was weighed; 3) data and analysis CMS developed and

considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS; 4) benefits and impacts considered; and 5) stakeholders, and other government agencies and organizations CMS engaged, formally or informally, in the process and how their input factored into the Agency's decision-making.

CIVIL MONETARY PENALTIES (CMPs) (Section 100)

- Complete notice-and-comment rulemaking on Program-related CMPs before seeking to impose any such CMPs on manufacturers.
- Implement procedures governing IRA drug pricing-related CMPs through a single rulemaking and model such procedures after well-established precedents.
- Do not impose CMPs on drug manufacturers for acts and omissions of third parties (e.g., secondary manufacturers, dispensers, providers, supply chain intermediaries) over which manufacturers have little, if any, control.
- Clearly explain, through notice-and-comment rulemaking, the factors CMS will consider in assessing whether to seek a Program-related CMP and the amount of any such CMP, and, during the early years of the Program, construe these factors liberally in favor of manufacturers in a manner that would not trigger a CMP.

PART D FORMULARY INCLUSION OF SELECTED DRUGS (Section 110)

- Minimize effects within therapeutic classes that would result in narrower formularies and fewer choices for patients.
- Review and update Part D formulary standards. Monitor plan coverage and tiering decisions, cost-sharing levels, and patient out-of-pocket exposure.
- Redefine Part D "negotiated price" to consider all manufacturer price concessions. Conduct strong oversight of formulary requirements and guard against non-discrimination violations.
- Re-examine and update rules around Part D coverage determinations, appeals, and tiering exceptions.

Our detailed comments follow below.

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Introduction

The Pharmaceutical Research and Manufacturers of America (PhRMA) believes that the "Medicare Drug Price Negotiation Program" (the Program), as codified in statute, will have significant consequences that will harm patients and continued biopharmaceutical innovation. In this regard, we are exceedingly disappointed that the Centers for Medicare & Medicaid Services' (CMS, the Agency) did not take steps in the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance or the Guidance)[7] to mitigate against the law's negative consequences. We urge the Agency to make changes to address this in revised Guidance.

As CMS revises the Guidance document, and implements the Program broadly, we urge the Agency to consider our recommendations to mitigate against harmful consequences for patients. We also strongly encourage CMS to continuously monitor and evaluate the impact of its policies on patient access to all medicines, including but not limited to selected drugs, and biopharmaceutical innovation, including innovation across a medicine's lifecycle. Below we describe concerns with government price setting in general before addressing the specific provisions of the Guidance.

The Impact of Price Setting on Patient Access and Biopharmaceutical Innovation

PhRMA is deeply concerned that setting prices for medicines will erode patient access and undermine continued biopharmaceutical innovation. Although national government price setting for medicines is novel for the U.S., it is not for other countries. Experience in these countries illustrates the degree to which government price setting erodes biopharmaceutical innovation and curtails patient access to treatments. Indeed, access delays and barriers are defining characteristics of such foreign systems, which prioritize cost-cutting over access, quality, and innovation. As a result, in countries that set prices for medicines, many patients – including those with cancer, diabetes, autoimmune, and rare diseases – face significant restrictions on access to treatments. Although the Inflation Reduction Act (IRA) differs from the price setting systems in these countries in several fundamental ways, the potential harm to patient access remains in any system in which the government is making a policy judgment related to a health intervention's benefits and costs at a national level.

Data on the availability of medicines in foreign countries underscores the challenges patients face as a result of price setting. For example, 85 percent of all new medicines launched between 2012 and 2021 are reimbursed in Medicare/Medicaid programs, compared to other countries' public health care programs where only 61 percent of new medicines are reimbursed in Germany, 48 percent in the United Kingdom, 48 percent in Japan, 43 percent in France, 24 percent in Australia, and 21 percent in Canada.[8] In these countries, it takes an average of 27 months longer than in the U.S. for new medicines to become reimbursed by a public plan.[9] The statistics underscore the importance of CMS implementing the Program in ways that help mitigate these potentially devastating effects.

In addition to potential harms to patient access for currently available treatments, government price-setting programs will invariably undermine incentives for biopharmaceutical innovation in the U.S. As a result of a health care system that relies on the strengths of market competition to balance cost control, patient access, and continued innovation, the U.S. leads the world in both research and development (R&D) for lifesaving treatments and cures. However, this was not always the case. In 1990, biopharmaceutical R&D investment in Europe was

[7] Available at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.
[8] PhRMA analysis of IQVIA MIDAS and country regulatory data, October 2022. Note: New active substances approved by FDA, EMA and/or PMDA and first launched in any country between January 1, 2012, and December 31, 2021. A medicine is considered publicly reimbursed in Canada if 50 percent or more of the population lives in a province where it is reimbursed by the public plan. A medicine is considered publicly reimbursed in the United Kingdom if recommended by England's National Institute for Health and Care Excellence (NICE) for funding by England's National Health Services (NHS).
[9] PhRMA analysis of IQVIA Analytics (2023).

more than 45 percent higher than similar investment in the U.S. However, decades of implementation of price controls and other anti-innovation policies across Europe pushed the locus of industry to the U.S., and as a result, reversed that dynamic.[10] In 2004, the U.S. Department of Commerce found that price controls in certain Organisation for Economic Co-operation and Development (OECD) countries suppress investment in worldwide R&D by 11 to 16 percent annually, which leads to fewer new medications being launched each year.[11] These effects likely have grown worse in the two decades since this research was published.

The IRA's drug price-setting provisions are already having an impact on biopharmaceutical R&D decisions. In the months following IRA passage, several biopharmaceutical manufacturers have announced cancellations of pipeline projects as a direct result of the law. A 2022 survey of PhRMA member company leaders shows that a majority have concerns – three-quarters of leaders responding to the survey said the IRA creates significant uncertainties for R&D planning and that they already are reconsidering R&D investment strategies, and 78 percent reported that early-stage pipeline projects are likely to be cancelled due to IRA provisions.[12] Fewer products in early-stage development will lead to fewer new cures and treatments for patients in the long run. Small molecule medicines, such as medicines for cancer that come in pill or tablet form, are particularly vulnerable to losing out on R&D investments, due to the short timeframe under which they can become eligible for price setting.[13] In the recent survey, 63 percent of respondents said they expect to shift R&D investment away from small molecule medicines.

While the price-setting framework in the IRA poses a threat to all biopharmaceutical innovation, it is particularly harmful to the R&D that occurs after a medicine's initial U.S. Food and Drug Administration (FDA) approval in the years leading up to and after a drug becomes eligible for price setting. In the aforementioned 2022 survey, 95 percent of respondents stated that they expect to develop fewer new uses for medicines due to the limited time available before a drug is subject to government price setting. The methodology for price setting should, to the extent possible, consider and preserve the intent of the intellectual property protections provided for companies to invest in biopharmaceutical R&D as well as the incentives for R&D that takes place after the initial FDA approval, including ongoing research that identifies important new uses of existing drugs.

There are numerous examples of medicines that have conferred benefit after their initial FDA approval. For example, an infused cancer drug originally approved via the accelerated approval pathway in 2014 to treat advanced or unresectable metastatic melanoma has since been approved for more than 35 different indications across 16 tumor types. This includes a recent FDA approval on January 26th, 2023 for adjuvant treatment following resection and platinum-based chemotherapy for stage IB, II, or IIIA non-small cell lung cancer (NSCLC).[14] This is the type of research and innovation CMS' implementation puts at risk.

Recent research further underscores the frequency at which post-approval innovation occurs. The Partnership for Health Analytic Research studied the development of improvements to medicines that received initial FDA approval between 2010 and 2012. Of these 88 medicines, more than half were later approved by the FDA for at least one additional indication. For cancer, the share was even higher; 62 percent of oncology medicines were

[10] Moll, N. (2020). Would the last pharmaceutical investor in Europe please turn the lights out. European Federation of Pharmaceutical Industries and Associations. Available at: https://www.efpia.eu/news-events/the-efpia-view/blog-articles/would-the-last-pharmaceutical-investor-in-europe-please-turn-the-lights-out/.
[11] U.S. Department of Commerce. (2004). Pharmaceutical Price Controls in OECD Countries: Implications for U.S. Consumers, Pricing, Research and Development, and Innovation. National Technical Information Service.
[12] Longo, N. (2023). WTAS: Inflation Reduction Act already impacting R&D decisions. PhRMA. Available at: https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions.
[13] Powaleny, A. (2023). IRA Impacts: Cancer treatment research and development. PhRMA. Available at: https://catalyst.phrma.org/ira-impacts-cancer-treatment-research-and-development.
[14] Keytruda [package inset]. Whitehouse Station, NJ: Merck & Co., Inc; 2023. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125514s128lbl.pdf.

later approved for one or more additional indications, a majority of which were approved seven or more years after approval.[15] Since the IRA creates disincentives for investment in indications post-original FDA approval, we suggest CMS give appropriate weight to post-approval innovations that deliver significant clinical benefit to patients, caregivers and society when determining Maximum Fair Prices (MFP) for selected drugs. In some instances, products with a number of indications that offer such significant benefit should be priced at or near the statutory ceiling.

PhRMA is also concerned about the potential impact of the IRA on orphan drug development, which often includes R&D on medicines for a rare disease that also might provide promise for non-orphan diseases with a related causal pathway. PhRMA notes that CMS has issued section 30.1.1 and its approach to determining eligibility for orphan drug exclusion in that subsection as final without accepting comments. Accordingly, as with the remainder of section 30, PhRMA is not commenting on the approach outlined in that subsection. PhRMA nevertheless notes CMS' statement that it "is considering whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development." PhRMA looks forward to engaging with CMS on this issue outside of the context of this Guidance process and encourages the Agency to issue guidance as expeditiously as possible, with appropriate opportunity for and consideration of public comment, on this important subject.

The aforementioned dangers to patient access to current and future treatments reinforce that CMS should design its methodology to mitigate negative effects on patients and continued innovation. CMS' MFP methodology should also reflect the reality that Part D sponsors already receive significant rebates on many drugs likely to be selected, and that the ceiling price set in statute can represent an additional deep discount to the Medicare program for these medicines.[16] Given the previously discussed consequences of price setting, CMS should be cautious when setting MFPs below the statutorily defined ceiling price. Setting prices for medicines is a highly complicated and technical undertaking that CMS must complete on an exceedingly short timeline and with limited existing expertise to build upon.[17] Challenges facing the Agency in this regard have also been acknowledged by CMS officials themselves, who have noted that the timelines are "tremendously tight for us."[18]

While we appreciate CMS taking the important step of issuing a Guidance, we note that it was published only five and a half months before the Agency is required to publish its list of ten selected drugs on September 1st, and only six and a half months before signed "Agreements" and complex, voluminous data submissions will be due from manufacturers. As a result, given these delays, we believe it is important for CMS to recognize the reality that neither the Agency nor manufacturers have a realistic period of time to prepare for implementation. In light of this, as described in more detail below, we believe CMS should commit to setting final MFPs at or near the deep, statutorily mandated "ceiling price" discounts in the first several years of the Program.

PhRMA also recommends that, consistent with longstanding principles of administrative law and good guidance, CMS respond in writing to comments on the Guidance, and that CMS maintain a public docket of comments received. Further, consistent with the timetable announced by CMS, we support completion and publication of

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[15] Ortendahl, J. D., Lee, J. S. (2022). Implications of the Inflation Reduction Act on Post-Approval R&D of Biopharmaceutical Medicines. Partnership for Health Analytic Research. Available at: https://www.pharllc.com/wp-content/uploads/2022/11/Clinical-Benefits-of-Post-Authorization-Research-Brief.pdf .

[16] CBO. (2021). A Comparison of Brand-Name Drug Prices Among Selected Federal Programs. Available at: https://www.cbo.gov/system/files/2021-02/56978-Drug-Prices.pdf; CBO (2023) How CBO Estimated the Budgetary Impact of Key Provisions in the 2022 Reconciliation Act. Available at: https://www.cbo.gov/system/files/2023-02/58850-IRA-Drug-Provs.pdf.

[17] As just one example, the Guidance states CMS will use a "qualitative" approach to consider on an indication-by-indication basis "nuanced differences between different drugs" on numerous dimensions of clinical performance, for a range of specific subpopulations. (Sections 50.2, 60.3.1, 60.3.3.1) CMS does not have a significant experience in performing and has not demonstrated its capability to perform such assessments. Moreover, this is only one of many novel areas for CMS that are part of price setting.

[18] Kelly, C. (2023). Medicare Price Negotiation: Data Needed to Establish 'Unintended Consequences' – CMS' Blum. Pink Sheet. Available at: https://pink.pharmaintelligence.informa.com/PS147732/Medicare-Price-Negotiation-Data-Needed-To-Establish-Unintended-Consequences--CMS-Blum?vid=Pharma&processId=0ad1a798-00c5-4c4b-b635-ace165a12f44.

Guidance with at least two months' lead time before the first list of selected drugs is announced on September 1st, 2023. We appreciate the Agency's reaffirmation in an April 7th communication that it plans to publish revised Guidance this summer, as well as its commitment to publicly posting the comments it receives.[19] In addition, we request to see the Agreement in advance of CMS' selection of drugs for price setting to give manufacturers opportunity to comment and time to review the Agreement in order to enter the price setting process.

Some of the flaws in the initial guidance appear to reflect a misperception that the Program represents a "negotiation" akin to manufacturer negotiations with health insurance companies. In fact, it is very different. Regardless of the term being used in statute, the Program is a federal policy decision-making exercise that involves both a non-public component (manufacturer submission of proprietary data and CMS communication directly with the company) and a public component (e.g., public solicitation of input to inform the Agency's decision and public explanation of the decision).

PhRMA's comments on specific provisions in the Guidance are set forth below. The recommendations are driven by our expertise on many of the issues on which CMS seeks comment and are offered to help mitigate against unintended and negative consequences to patients and innovation. We urge CMS to revise its Guidance in response to the below recommendations.

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I. Requirements for Manufacturers of Selected Drugs (Section 40)

Section 40 of the Guidance focuses on the "Agreement" that manufacturers must enter with CMS under the Program and other issues related to the Agreement. PhRMA is concerned that several provisions in this section exceed CMS' statutory authority, are unworkable, and contribute to a decision-making framework that is subjective and unpredictable. We describe these concerns, and recommend modifications, in more detail below.

a. Primary/Secondary Manufacturer Definition

CMS' proposal to establish separate categories of "Primary" and "Secondary" manufacturers, and to hold Primary Manufacturers responsible for other distinct corporate entities ("Secondary" manufacturers), is unworkable and not supported by statute. In section 40, CMS notes that the IRA adopts the definition of "manufacturer" in section 1847A(c)(6)(A) of the Social Security Act (SSA) (which derives from the Medicaid rebate statute).[20] CMS then explains that the IRA directs it to negotiate an MFP with "the manufacturer" of a selected drug.[21] If "more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of [initial price applicability year (IPAY)] 2026," CMS states, it "intends to designate the entity that holds the [New Drug Application(s) (NDA(s)) / Biologic License Application(s) (BLA(s))] for the selected drug to be 'the manufacturer' of the selected drug (hereinafter 'Primary Manufacturer')." Any other entity that meets the statutory definition of manufacturer for a drug product included in the selected drug and "either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets the selected drug pursuant to an Agreement with the Primary Manufacturer" would be deemed a "Secondary Manufacturer." Secondary Manufacturers would include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that "meet these criteria."

CMS proposes to sign an Agreement only with the Primary Manufacturer, under which CMS states that the Primary Manufacturer would be required to agree, among other things, to:

[19] Centers for Medicare & Medicaid Services. (Email announcement, received April 7, 2023). Medicare Drug Price Negotiation Initial Guidance: Comments due by April 14.
[20] SSA § 1191(c)(1), incorporating 1847A(c)(6)(A), incorporating § 1927(k)(5).
[21] SSA § 1193(a)(1).

- Report manufacturer-specific information applicable to any Secondary Manufacturer (and in some cases to blend pricing data of the Secondary Manufacturer with its own pricing data);[22]
- Ensure that any Secondary Manufacturer(s) make the MFP available to MFP-eligible individuals and to pharmacies, mail order services, and other dispensers;
- Respond to CMS requests within "specified timeframes" with documentation demonstrating compliance and remedial actions, as applicable, pursuant to reports of noncompliance or other CMS compliance and oversight activities; and
- Pay any CMPs for violations (including those stemming from noncompliance by any Secondary Manufacturer).

Other than citing to use of the word "the," CMS cites to no other statutory authority for imposing vicarious liability on Primary Manufacturers. And the provision immediately preceding the paragraph referencing "the manufacturer" mentions multiple Agreements with multiple manufacturers, stating that the "Secretary shall enter into Agreements with manufacturers of selected drugs."[23] The reference to "the" manufacturer, thus, merely refers back to each Agreement CMS maintains with each of the various manufacturers signing these Agreements. If more than one legally distinct entity meets the definition of "manufacturer," then CMS may enter into separate Agreements with each of such manufacturers, and there would be one "manufacturer" or "the manufacturer" under each Agreement. As a result, Congress' use of "the" hardly merits the significance CMS reads into it, and certainly does not warrant adopting a policy that conflicts with ordinary corporate responsibilities.[24]

Nothing in the IRA authorizes CMS to impose requirements, liability, or certainly not excise taxes, on a legal actor who maintains a distinct corporate identity. While CMS may argue that the IRA permits adding requirements "determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program,"[25] CMS' proposal goes beyond anything "necessary" to administer the MFP program. In fact, CMS arguably could monitor a manufacturer's compliance more easily if it maintains an Agreement with each distinct corporate entity – such that it is directly, rather than indirectly, holding each entity accountable.

Any other reading of the language would amount to Congress delegating to CMS major corporate law questions of holding one entity responsible for the activities of an unrelated corporate actor, even though there is no indication in the IRA that Congress intended to grant the Secretary powers so extensive as to alter ordinary laws of corporate liability, or to require amendments to the contracts Primary Manufacturers currently maintain with Secondary Manufacturers. Even if Congress had delegated such broad authority, gap-filling rules that alter contracts and corporate legal assumptions would require more than mere guidance.[26]

CMS' proposal also conflicts with past practice. Historically, CMS has not required manufacturers to report Secondary Manufacturers' data. CMS decided not to finalize such a proposal in a 2007 rule, after receiving comments that doing so would be "unduly burdensome on manufacturers, call into question the veracity of manufacturer pricing information reported to CMS, and potentially violate anti-trust statutes because [the CMS proposal] would require manufacturers to share pricing information and engage in anti-competitive practices."[27]

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[22] Guidance at Appendix C; ; Negotiation Data Elements under sections 11001 and 11002 of the Inflation Reduction Act ICR. Available at: https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847.
[23] SSA § 1193(a) (emphasis added).
[24] See also 1 U.S.C. 1, which provides that, "[i]n determining the meaning of any Act of Congress, unless the context indicates otherwise—words importing the singular include and apply to several persons, parties, or things; [and] words importing the plural include the singular. . . ."
[25] SSA § 1193(a)(5).
[26] *Perez v. Mortg. Bankers Ass'n*, 575 U.S. 92 (2015) (Guidance cannot have the force and effect of law).
[27] 72 Fed. Reg. 39199 (Jul. 17, 2007).

CMS concluded that requiring a primary manufacturer to include sales of a secondary manufacturer within its Average Manufacturer Price (AMP) calculation "would be problematic from an administrative accounting and anti-trust perspective."[28]

As was the case in 2007, it would be legally problematic, as well as infeasible, for innovator manufacturers to gather the vast amounts of data CMS is anticipating gathering – all prior to CMS' October 1st, 2023 deadline for signing an Agreement under section 1193 with the Primary Manufacturer and October 2nd, 2023 deadline to submit extensive data and research to CMS. To report information to CMS, innovator manufacturers would likely have to access proprietary books and records of the Secondary Manufacturers, which may be competitors, raising a variety of business and legal issues. For example, section 50.1, explains that the Primary Manufacturer is required to submit "[c]urrent unit costs of production and distribution of the selected drug, averaged across the Primary Manufacturer and any Secondary Manufacturer(s)." Section 50.1 also anticipates that the Primary Manufacturer will collect "[m]arket data and revenue and sales volume data" from Secondary Manufacturers and blend the data with its own data. Section 50.1.1 states that the Primary Manufacturer "must submit data on [non-Federal average manufacturer price (non-FAMP)] for the selected drug for the Primary Manufacturer and any Secondary Manufacturer." The Guidance, if adopted as final, raises the specter of anti-trust concerns to the extent it requires a Primary Manufacturer to collect and aggregate non-public, competitively sensitive Secondary Manufacturer information otherwise not accessible by the Primary Manufacturer.

Further, even if Primary Manufacturers could modify existing contractual agreements to ensure indemnification clauses, create firewalls to access proprietary information, and ensure information is available, there is simply insufficient time to do so prior to the deadlines for the 2026 IPAY (which require execution of CMS-manufacturer Agreements under section 1193 by October 1st, 2023, and certain information to be submitted by October 2nd, 2023). Indeed, it is not clear what unintended consequences CMS' policy would have on the supply chain and/or collaboration among manufacturers to spur innovation, and CMS includes no discussion of how its requirements would affect current repackaging, relabeling, or authorized generic manufacturing activities.

For the reasons stated above, ***CMS must not adopt the Primary/Secondary Manufacturer policy.*** If more than one entity meets the definition of manufacturer, CMS may enter into separate Agreements with each manufacturer, as the statute already anticipates multiple Agreements with multiple manufacturers.

b. Entrance into Agreement with CMS and Compliance with Administrative Actions (Sections 40.1 and 40.5)

CMS states that it would use the Health Plan Management System to identify relevant points of contact, effectuate the Agreement, and store the Agreement, and that within "5 days following publication by CMS of the list of selected drugs for an initial price applicability year [September 1st, 2023, for the first year of the Program], if the Primary Manufacturer of a selected drug elects to enter into an Agreement with CMS…the Primary Manufacturer must submit to CMS all names, titles, and contact information for representatives authorized to execute the Agreement and conduct the negotiation." CMS also notes that it "intends for the Agreement to contain the requirements discussed in sections 40.1 through 40.7 of this memorandum." While CMS states it "will make reasonable efforts to make the final text of the Agreement available to the public before the selected drug list for initial price applicability year 2026 is published," it has publicly indicated it will not likely seek comments on the Agreement itself. As the deadline for publication of the selected drug list is September 1st, 2023, CMS' proposal for "final text" appears to mean that manufacturers will be required to sign, within a month (by October 1st, 2023), an Agreement they have never seen before and which they have only 30 days to review.

First, ***PhRMA recommends that CMS should not adopt its "5 days for review and decision" proposal.*** The statute (which gives as little as 30 days post-selection to decide whether to sign) is itself highly problematic, but

[28] Ibid at 39200.

does not authorize CMS to cut the 30-day decision period down to five days.[29] While PhRMA appreciates CMS attempting to identify authorized representatives early, requiring manufacturers to decide whether to "elect to sign" within five days would conflict with the statute's later deadline of October 1st. Moreover, as long as an Agreement may be signed by the statutory deadline, CMS should view statutory obligations as fulfilled.

Second, ***PhRMA reminds CMS that it may not impose manufacturer requirements that go beyond the plain language of section 1193 of the SSA.*** Although in several places, CMS characterizes the Agreement as "voluntary" it is important to note that the IRA price-setting provisions are distinct from an ordinary contract or grant relationship, where an entity submits a bid or proposal in response to a solicitation. The 1193 Agreement cannot be described as voluntary. Instead, the Agreement is properly understood as a contract of adhesion, signed under duress. Manufacturers of selected drugs have little recourse other than to sign the Agreements. If the manufacturer does not enter into the Agreement by the required date (October 1st, 2023, for the first year of the Program), the manufacturer is subject to per-day excise taxes starting at almost twice the sales of the selected drug and increasing to 1,900 percent of a drug's total revenues.[30] While this up-to 1,900 percent assessment is framed as a "tax," Congress understood that it would function as a penalty forcing manufacturers to subject themselves to the government's so-called "agreement." For example, the Joint Committee on Taxation estimated that the "tax" would raise zero revenue, because no manufacturer could possibly afford to pay such an astronomical assessment.[31] Further, to suspend imposition of the possibility of crippling excise taxes under the IRA, a manufacturer must terminate "all" applicable agreements under Medicaid and Medicare Part D,[32] resulting in the termination of coverage in Medicaid and Medicare Parts B and D for all of the manufacturer's products – not just the selected product – when almost half of annual nationwide spending on prescription medicines is through Medicare and Medicaid.[33]

Because the IRA sidesteps a true negotiation in any sense of the term, CMS cannot use the Agreement to bind manufacturers to requirements that go beyond the plain language of section 1193 and claim manufacturers "agreed" to the terms. CMS has also previously noted that statutory agreements that function similar to the 1193 agreement are not "contracts" or true "agreements" but merely a notification of the statutory provisions governing the Program. With respect to the Medicaid National Drug Rebate Agreement (NDRA), CMS noted:

> The NDRA is not a contract. Rather, it should be viewed as an opt-in Agreement that memorializes the statute and regulations. Therefore, we noted our intention to use the updated NDRA as a standard agreement that will not be subject to further revisions based on negotiations with individual manufacturers.[34]

Third, ***PhRMA recommends CMS share the Agreement text itself for a meaningful period of comment.*** Without seeing the Agreement text and being afforded a period of comment, it is unreasonable for CMS to conclude that innovator manufacturers will simply review and sign, all in a one-month period. In past situations,

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[29] SSA §§ 1191(b)(4)(A); 1191(d)(2). In other cases, those entering into agreements have more time to review. The Coverage Gap Discount Program agreement allowed a 30-day review period. The VA offers a rolling submission process. The Medicaid rebate program has another approach that implements the agreement 60 days after the end of the quarter. *See e.g.,* 42 CFR § 423.2315(c); https://www.medicaid.gov/medicaid/prescription-drugs/medicaid-drug-rebate-program/medicaid-national-drug-rebate-agreement-ndra/index.html; https://www.va.gov/opal/nac/fss/pharmaceuticals.asp;https://www.va.gov/opal/docs/nac/fss/vaSolicitationM5Q50A03R8.zip.

[30] 26 U.S.C. 5000D(b)(1)(A). See also Congressional Research Service, *Tax Provisions in the Inflation Reduction Act of 2022,* tbl. 2 (2022) (confirming a top excise tax of 1,900 percent).

[31] Joint Commission on Taxation, *Estimated Budget Effects of the Revenue Provisions of Title XIII - Committee On Ways And Means, of H.R. 5376, The "Build Back Better Act," As Passed by the House of Representatives, Fiscal Years 2022–2031*, at 8 (Nov. 19, 2021), https://bit.ly/3plC4cd ("no revenue effect"); *accord* Letter from P.L. Swagel, Director, CBO, to Hon. F. Pallone Jr., Chairman, Committee on Energy and Commerce (Oct. 11, 2019), at 14. Available at: https://bit.ly/3osZPzX (noting JCT had concluded, of identical predecessor provision, that "manufacturers would either participate in the negotiation process or pull a particular drug out of the U.S. market entirely").

[32] 26 U.S.C. 5000D(c).

[33] CBO. Prescription Drugs: Spending, Use, and Prices at 8 (2022).

[34] 83 Fed. Reg. 12770, 12771 (March 23, 2018).

CMS has provided the text of the draft agreement and requested comments before finalizing the agreement.[35] Without knowing exactly how the Agreement will read for this Program, it is not possible to anticipate every potential comment on the contours of the Agreement.

Fourth, and finally, ***PhRMA recommends CMS not include in the Agreement open-ended language that seeks to bind manufacturers to unknown requirements or ambiguous terms.*** CMS states in section 40.5 that "after entering in an Agreement with CMS…the Primary Manufacturer must comply with requirements determined by CMS to be necessary for purposes of administering the Negotiation Program and monitoring compliance with the Negotiation Program." CMS does not offer additional information as to what exactly it intends to include as a result of this statement. However, even if the Agreement were a true contract – which, as discussed above, it is not – parties to a contract cannot be "bound to unknown terms which are beyond the range of reasonable expectation."[36]

c. Submission of Data to Inform Negotiation (Section 40.2)

Under the timetable described in the Guidance, manufacturers of selected drugs will only have 30 days after the list of selected drugs is published to prepare and submit information to CMS. Thirty days is a woefully inadequate period of time for manufacturers to gather and submit the data that will be used in price setting. CMS has authority to allow flexibility on submission of data beyond October 2nd, 2023, and should use that authority to provide additional time for manufacturers to submit robust data and research to support MFP determinations. CMS or manufacturers may also find that there must be an opportunity to submit additional information to resolve issues, answer specific questions, or address misunderstandings in how CMS is interpreting data or data submission requirements. The deadline of October 2nd, 2023 arguably applies only to the data specifically mentioned in section 1193(a)(4) (that is, non-FAMP data). This analysis would harmonize the following statutory provisions:

- Section 1194(b)(2)(A), which, as amended by 1191(d)(5), states "Not later than October 2, 2023, the manufacturer of the drug shall submit to the Secretary, in accordance with section 1193(a)(4), the information *described in such section*" (emphasis added);
- Section 1193(a)(4), which "describes" non-FAMP information as well as "information that the Secretary requires to carry out the negotiation (or renegotiation process) under this part"; and
- Section 1194(e), which requires certain information for price setting, but is <u>not</u> cross-referenced in section 1193(a)(4).

The IRA also states that the Secretary may specify the "manner" in which data are submitted. The fact that the statute fails to "describe" an October 2nd, 2023 deadline for submitting data to support consideration of the section 1194(e) factors, along with the discretion the Secretary maintains to dictate the manner of submission, allows CMS some flexibility on timelines. This flexibility provides the Agency an important opportunity to facilitate a more effective implementation of the Program by permitting submission of additional or updated data and research after October 2nd. ***PhRMA recommends that CMS read the statute in a manner that ensures adequate time to gather information and submit data on the 1194(e) factors, and not to adhere to an arbitrary and rigid deadline of October 2nd if there are other, more reasonable ways to interpret the language***. Further, we urge the Agency to specify opportunities for manufacturers to submit additional data after October 2nd, including manufacturer-specific data under section 1194(e)(2).

d. Confidentiality of Proprietary Information (Section 40.2.1)

[35] 81 Fed. Reg. 78816 (Nov. 9, 2016).
[36] Restatement (Second) of Contracts § 211 (1981).

PhRMA appreciates CMS' recognition that a large amount of the data to be submitted by manufacturers, including non-FAMP data[37], is highly sensitive and proprietary. In Appendix C, CMS includes ten pages of definitions relating to "manufacturer-specific" information to be submitted by October 2nd, 2023. Separately, CMS recently released a 45-page form for collecting information.[38] Despite these robust submission requirements, the Guidance fails to describe, and therefore does not provide opportunity for comment on, the details of the robust confidentiality policy that must accompany companies' submission of manufacturer-specific data. We discuss this concern in more detail below and provide suggested minimum requirements for a confidentiality policy.

PhRMA is unaware of any other program that would compile such a large volume of biopharmaceutical innovator information in one repository – on R&D, patent, cost, pricing, and other highly sensitive data. Congress seemingly was aware of the sensitivity of data to be submitted, as it included in the IRA an unusually restrictive limitation, applying not just to disclosure of manufacturer-submitted data but also their "use." Only the Secretary (or Comptroller General in certain situations) may use the data, and then, only to carry out the price-setting Program.[39]

While CMS acknowledges it will adopt a confidentiality policy, it does not propose such a policy for comment, and states only that such policy would be "consistent with existing requirements for protecting proprietary information, such as Exemption 4 of the Freedom of Information Act (FOIA)." However, Exemption 4 of FOIA addresses disclosure, not use, and nothing in the IRA directs CMS to use FOIA as the basis for its confidentiality and security protocols. Further, Exemption 4 would not by itself adequately protect the proprietary information the IRA requires. While PhRMA urges CMS to adopt the procedures of FOIA regulations allowing innovators to designate part or all of the information submitted as proprietary,[40] CMS must also develop a robust confidentiality policy, shared with manufacturers for feedback.

CMS' cursory, one-line explanation of a "confidentiality policy" provides little assurance to manufacturers that their highly valued information will be protected. At a minimum, any confidentiality policy must require:

- Access to any information received is limited to the smallest number of employees and other personnel possible, as well as the minimum data necessary, and such personnel are inventoried and recorded on a regular basis (including an explanation of such individual's legitimate need to use the information and purpose);
- Execution of non-disclosure agreements by any individuals with access to the data (including contractors and staff) as a pre-condition to access, under which they are restricted from improperly using or disclosing any proprietary information received, during their employment/engagement and in perpetuity post-employment;
- Destruction of data by any individuals with access to the data when any Agreement terminates. CMS, the Comptroller General, or any part of the U.S. Department of Health and Human Services (HHS) that accesses information maintains policies as to how and when it will destroy proprietary information of the manufacturer, informs the manufacturer of such destruction, and documents compliance with destruction policies;

[37] Non-FAMP is the average price paid by wholesalers for drugs distributed to non-federal purchasers. Manufacturers calculate this on a quarterly basis and report it to the U.S. Department of Veterans Affairs (VA); this calculated price includes any rebates, cash discounts or other price reductions but excludes any discounts given to federal purchasers. Manufacturer rebates, discounts, and other price reductions are confidential and proprietary and non-FAMP, as used today with the VA, is not a publicly available metric.
[38] 88 Fed. Reg. 16983 (March 21, 2023); https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847.
[39] SSA § 1193(c).
[40] 45 C.F.R. § 5.41.

- Notification to any submitters of any erroneous use or disclosure of proprietary information, even if inadvertent, and how it intends to remedy such use or disclosure;
- Notification to manufacturers any time data are shared outside of CMS (for example with a contractor) or CMS intends to use such data for purposes unrelated to price setting (for example, because CMS determines the data are not proprietary), the rationale for such sharing/use, and providing manufacturers with a robust prior opportunity to object to such sharing/use, along with an adjudication process. If CMS determines that otherwise proprietary information is nevertheless "publicly available," CMS should explain such reasoning prior to allowing such information to be used (and provide for a period of adjudication before the data could be shared or released). Again, such notification must extend not just to public disclosure, but also any "use" or disclosure outside CMS, including to Congress or other agencies; and
- Referrals made to the Department of Justice regarding violations of criminal laws prohibiting the publication, divulging, disclosure, or making known in any manner or to any extent not authorized by law, trade secret or confidential commercial information.[41]

The government has a history of requiring non-disclosure agreements from contractors and others under agreement, and PhRMA is happy to share templates. Exhibit B, attached to this comment letter, is one such template. Clauses CMS should add to any contracts or other Agreements include HHS Acquisition Regulations (HHSAR) 352.224-71, and clauses similar to H.6, or the "Disclosure of Information" provision, respectively, at the sites below:

- https://www.hhs.gov/sites/default/files/gram-contract.pdf; and
- https://www.hhs.gov/sites/default/files/vaccine-agreement-with-glaxo-smith-kline-modifications-1-and-2.pdf.

CMS should put forward a security policy as well, explaining how it will ensure the cybersecurity of systems holding manufacturer-specific data. The security protocol must include limited access to only certain personnel via secure portal; procedures on secure encrypted transmission mechanisms (as approved by HHS' Chief Information Officer and Office of the General Counsel); secure storage; inability to download confidential information to removable media or any other portable storage; policies on and tracking of any printing or screenshotting of confidential information (including watermarking of electronic and paper copies with a "confidential" label, safeguards that only a minimum amount may be printed, and standards that printouts remain within a particular physical location from which they cannot be removed, along with locked offices and file cabinets).

CMS should periodically audit and report on its use of confidential commercial information, as well as compliance with its confidentiality and security protocols.

For the reasons stated above, ***PhRMA recommends that CMS protect confidential information beyond the protections of FOIA Exemption 4, share its confidentiality policy for comment, and ensure contractors and others with access to manufacturer data have agreements with CMS that adequately protect the high volumes of proprietary information CMS will collect.***

PhRMA also asks that CMS clarify that the existence of and status of a pending NDA or BLA, in addition to information contained in a pending NDA or BLA, will be treated as proprietary information under SSA section

[41] 18 U.S.C. 1905.

1193(c) and as trade secret and/or confidential commercial information that is protected from disclosure under Exemption 4 of the FOIA, 5 U.S.C. § 552(b)(4).

This clarification is needed because section 40.2.1 of the Guidance states that "CMS intends to treat the data on prior Federal funding and approved patent applications, exclusivities, and *applications and approvals* under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Services Act as non-proprietary because CMS believes these data are available publicly." The use of the term "applications and approvals" suggests that both pending and approved applications might be treated as non-proprietary. The "applications and approvals" language also appears in Appendix C (Definitions), which states that "[a]ctive *and pending* FDA applications and approvals includes…all applications for approval under section 505(c) of the Federal Food, Drug, and Cosmetic Act or sections (sic) 351(a) of the Public Health Service Act, *including those not yet decided*…" (emphasis added).

PhRMA disagrees that "these data are available publicly." On the contrary, information in pending marketing applications is typically proprietary and highly sensitive and is protected from disclosure by federal law. This sensitivity remains after approval, with much data and information in approved applications remaining protected confidential commercial information and trade secrets exempt from disclosure. Under FDA's regulations, the existence and status of a pending application, in addition to information contained in a pending NDA or BLA, generally are protected from public disclosure.[42] FDA adopted this regulation to implement the Federal Trade Secrets Act, FOIA, and section 301(j) of the FD&C Act, which all protect such information from public disclosure, and has long regarded this information as competitively sensitive for which disclosure would cause competitive harm.[43] Only once a decision on an application is final will certain information regarding the application be subject to potential disclosure, and even then, other information within the application remains protected.[44] Consistent with the fact that FDA protects information about and in pending marketing applications from disclosure, CMS' Guidance should be revised to provide that CMS will treat such information as proprietary under SSA section 1193(c) and as trade secret and/or confidential commercial information under FOIA. Indeed, the fact that CMS has misidentified these data as publicly available further underscores the need to rely upon a manufacturer's indication that data are proprietary and not in the public domain.

Finally, CMS notes that it will publish an explanation for the MFP by March 1st, 2025, and may make "high-level comments about the data submitted to CMS, without sharing any proprietary information," such as saying that the "manufacturer has recouped its R&D costs." In making any such high-level statement, the Agency should be specific about its limitations.[45] CMS is defining R&D in ways that differ from the ways that the biopharmaceutical industry does. The industry definition as a matter of course includes costs for all failures and

[42] See 21 C.F.R. §§ 314.430(b) ("FDA will not publicly disclose the existence of an application…before an approval letter…or tentative approval letter is sent to the applicant…, unless the existence of the application…has been previously publicly disclosed or acknowledged."); id. § 314.430(c) ("If the existence of an unapproved application or abbreviated application [for a small molecule drug] has not been publicly disclosed or acknowledged, no data or information in the application or abbreviated application is available for public disclosure."); id. § 601.51(b) ("The existence of a biological product file will not be disclosed by [FDA] before a biologics license application has been approved unless it has previously been publicly disclosed or acknowledged."), id. § 601.51(c) ("If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure."); see also 39 Fed. Reg. 44,602, 44,634 (Dec. 24, 1974) ("The existence of a pending NDA constitutes confidential commercial information where the existence of clinical testing has not previously been publicly disclosed or acknowledged.")

[43] 39 Fed. Reg. at 44,634

[44] 21 C.F.R §§ 314.430(f), (g), 601.51(e), (f)

[45] CMS should also remain mindful of international commitments to protect undisclosed information from being disclosed or unfairly used, particularly under Article 39 of the WTO TRIPS Agreement. Failure to protect confidential information, including in any "high-level" statements, would be contrary to international commitments of the United States.

successes and doesn't distinguish between them.[46] Thus, "high-level" statements should not provide misleading information that extends beyond CMS' unique definitions and its price-setting scheme.

e. Data Use Provisions and Limitations (Section 40.2.2)

PhRMA strongly opposes provisions of the Guidance that would prohibit manufacturers from disclosing information exchanged verbally or in writing that relates to basic elements of CMS' MFP decision-making process. These provisions lack legal authority, hinder government accountability, and prevent ongoing, year-to-year learning that will be important to the effective implementation of and manufacturer compliance with the Program. We urge CMS to delete these provisions and adopt an approach that promotes transparency and accountability in government decision-making while protecting proprietary and confidential information.

Specifically, in section 40.2.2 of the Guidance, CMS cites to general authority for "administering the program and monitoring compliance," to propose a sweeping policy that would restrain manufacturer speech by placing limits on what a manufacturer can use or disclose from CMS' offers, including the ceiling price, the information contained in any concise justification provided with an offer, and any information exchanged verbally during the "negotiation" period. CMS would prohibit audio or video recording of any oral conversations between CMS and a manufacturer, and even limit use – stating that manufacturers could use government information only for purposes of the Program, and as required by applicable state or federal law.

The Agency also proposes a "Certificate of Data Destruction," to be submitted within 30 days of a drug or biologic no longer qualifying as a selected drug. Under such certificate, a manufacturer would certify that all information received from CMS during the "negotiation" period and potential "renegotiation" period(s), including the initial offer and any subsequent offers, and the concise justification(s), and any of the manufacturer's written notes or emails pertaining to negotiation (or renegotiations) with CMS, have been destroyed.

PhRMA is unaware of CMS or HHS ever having proposed such an over-broad and patently unconstitutional information policy. Prior governmental restraints on speech "are the most serious and the least tolerable infringement on First Amendment rights,"[47] and they are subject to a "heavy presumption against [their] constitutional validity."[48] Indeed, restraints on the disclosure of "truthful information about a matter of public significance" – like the data subject to use restrictions in section 40.2.2 – are almost never permissible under the First Amendment.[49] The Supreme Court has recognized a limited exception to that rule for information that cannot be disclosed without doing substantial, concrete, and immediate harm, such as when necessary to protect "the secrecy of information important to our national security."[50] However, the information at issue here is plainly not of that type.[51]

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[46] PhRMA's definition of R&D expenditures reported in its Annual R&D Survey (https://phrma.org/resource-center/Topics/Research-and-Development/2022-PhRMA-Annual-Membership-Survey) includes basic and applied research, as well as developmental activities carried on or supported in the pharmaceutical, biological, chemical, medical, and related sciences, including psychology and psychiatry, if the purpose of such activities is concerned ultimately with the utilization of scientific principles in understanding diseases or in improving health. When reporting industry R&D expenditures, members include the total cost incurred for all pharmaceutical R&D activities including salaries, materials, supplies used, a fair share of overhead (administration, depreciation, space charges, rent, etc.), as well as the cost of developing quality control. Also included are expenditures within the company's U.S. (inside)/foreign (outside) research laboratories plus R&D funds contracted or granted to commercial laboratories, private practitioners, consultants, educational and nonprofit research institutions, manufacturing and other companies, or other research-performing organizations located inside/outside of the United States. These **do not** include the cost of routine quality control activities, capital expenditures, or any costs incurred for drug or medical R&D conducted under a grant or contract for other companies.

[47] *Nebraska Press Ass'n v. Stuart*, 427 U.S. 539, 559 (1976).

[48] *Org. for a Better Austin v. Keefe*, 402 U.S. 415, 419 (1971) (quotation marks omitted).

[49] *Bartnicki v. Vopper*, 532 U.S. 514, 527 (2001) (citation omitted).

[50] *Snepp v. United States*, 444 U.S. 507, 509 n.3 (1980).

[51] *See McGehee v. Casey*, 718 F.2d 1137, 1141 (D.C. Cir. 1983) ("The government has no legitimate interest in censoring unclassified materials.").

Indeed, section 40.2.2 does not claim that its data use restrictions would satisfy strict scrutiny – i.e., that they serve a compelling state interest and are narrowly tailored to achieve that interest. Much less does CMS offer actual "empirical evidence" to substantiate the need for such restrictions,[52] nor can CMS defend the data use restrictions in section 40.2.2 on the ground that manufacturers enter the price setting process voluntarily. In fact, as noted above, participation by manufacturers is not truly voluntary, as the manufacturer's ability to opt out of the program is highly limited, both as a practical and legal matter. But even if participation were voluntary, "[t]he government may not censor [truthful, non-classified information], 'contractually or otherwise.'" [53] Simply put, the government may not impose a "direct regulation of speech…as a condition on the receipt of federal funds" where, as here, the condition goes "beyond ensuring that federal funds [are] not…used to subsidize" unwanted speech.[54]

Section 40.2.2's document-destruction requirements similarly constitute impermissible restrictions on the freedom of speech. Indeed, the requirement to destroy information "receive[d] during the negotiation period from CMS" goes a significant step further even than a prior restraint on publication. It is hard to imagine almost any scenario (outside the national security context) in which the government can justify forcing a private individual to destroy the individual's own property – even the individual's own notes – in order to prevent truthful information from getting out. Taken literally, the Guidance would require manufacturers to destroy emails, notes, and other records of their own internal company deliberations, so long as those deliberations "pertain[] to negotiations," regardless of whether the records reflect information from CMS itself. As noted below, the policy would also prevent manufacturers from reporting inappropriate or unlawful behavior by CMS or its employees and officials, since such disclosures are usually not "required by applicable state or federal law." The government has no legitimate interest – much less a compelling interest – in commanding such a result.

Section 40.2.2 violates the First Amendment in other ways as well. The prohibition on using price setting data "for any purpose other than the Medicare Drug Negotiation Program" is impermissibly vague. Vague laws inherently invite subjective enforcement, a concern that is heightened when speech is at issue.[55] For that reason, "a more stringent vagueness test" applies where, as here, the government attempts to restrict private speech.[56] If taken at face value, CMS' prohibition would apply to a manufacturer's internal deliberations, akin to an individual's internal thought process; such a prohibition would be substantially overbroad and would fail strict scrutiny. But even if CMS would read the prohibition more narrowly – something it is not possible to discern from the Guidance itself – the Guidance's failure to specify its scope with reasonable precision threatens to chill legitimate speech and invites arbitrary enforcement.[57]

For information that is not proprietary to the manufacturer, the proposal also is at odds with government records retention and freedom of information principles. For example, for non-proprietary information held in government custody, the government ordinarily is required to disclose such data if requested under FOIA.[58] Thus, while information *held by the government* might be subject to records requests under FOIA, CMS would simultaneously require a *manufacturer* to hide or destroy the same information. Presumably, when the information is in government custody, it would be subject to Federal Records Act[59] requirements, under which the Agency would be required to maintain the records, document its activities, file records for safe storage and efficient retrieval, and dispose of records only according to an Agency schedule.

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[52] *United States v. Playboy Enter. Grp., Inc.*, 529 U.S. 803, 816 (2000).
[53] *McGehee*, 718 F.2d at 1141 (quoting *United States v. Marchetti*, 466 F.2d 1309, 1313 (4th Cir. 1972)).
[54] *Agency for Intern'l Dev. v. Alliance for Open Society Intern'l, Inc.*, 570 U.S. 205, 213-15 (2013).
[55] *See Grayned v. City of Rockford*, 408 U.S. 104, 109 (1972) ("[W]here a vague [law] abuts upon sensitive areas of basic First Amendment freedoms, it operates to inhibit the exercise of those freedoms.") (cleaned up).
[56] *Village of Hoffman Estates v. Flipside, Hoffman Estates, Inc.*, 455 U.S. 489, 499 (1982).
[57] *See Grayned*, 408 U.S. at 108-09.
[58] 5 U.S.C. 552.
[59] 44 U.S.C. 31.

Far from allowing CMS to "administer the program" and "monitor compliance," the provisions would have the effect of undermining sound program administration and consistent compliance by foreclosing vital opportunities for program transparency. Manufacturers that undergo the MFP decision-making process would effectively be muzzled from pointing out flaws, oversights, or methodological problems in CMS' administration of the Program or its compliance monitoring. Further, CMS' proposal would impede the year-to-year learning by stakeholders that would serve an important role in effective program administration and compliance.

It is unclear if the policy would apply to sharing or retaining information with respect to attorneys, accountants, or others performing due diligence on a company's activities or providing the company with legal advice. Even within the same corporation, a manufacturer would not have the data to inform activities on a second set of selected drugs. The degree of secrecy imposed by these provisions creates the impression of an Agency unwilling to subject its decisions to open, evidence-based scrutiny, creating a significant risk of undermining public trust in CMS decision-making. With the public explanation of the MFP occurring many months after the end of the price setting period (on March 1st, 2025) and a full 17 months after the sole, limited opportunity for the public to provide input, the public and those relying on medicines or certain forms of medicines that could be affected by CMS price setting may question why CMS felt the need to shield its decision-making process from scrutiny in this way. ***For the reasons stated above, CMS should abandon the proposed data use restrictions on disclosing and/or using government-provided data as the policy violates the First Amendment, conflicts with government transparency principles, and cannot be finalized.***

In a recent blog-post CMS stated: "CMS continues to believe that transparency promotes accountability."[60] We agree, and believe such transparency must start with the Agency itself.

f. Effectuation of the MFP (Section 40.4)

Under section 1193(a) of the SSA, manufacturers entering into an Agreement with CMS must provide access to the MFP for selected drugs that are covered under Part D to (1) MFP-eligible individuals and (2) pharmacies, mail order services, and other dispensers with respect to such MFP-eligible individuals who are dispensed such drugs. CMS notes in the guidance that the IRA requirement that the negotiated price for a selected drug be less than or equal to the MFP plus a dispensing fee for MFP-eligible individuals[61] "ensures that Part D MFP-eligible individuals will have access to the MFP at the point-of-sale."[62] In addition, CMS would define "providing access to the MFP" in the context of dispensing entities as ensuring the amount paid by the dispensing entity is not greater than the MFP. Furthermore, CMS intends to require Primary Manufacturers to provide access to the MFP in one of two ways: (1) by ensuring that the price paid by the dispensing entity is no greater than the MFP; or (2) by providing retrospective reimbursement for the difference between the dispensing entity's actual acquisition cost and the MFP.[63]

It is critical that the Agreement reflect such options and ensure that manufacturers are only required to provide access to the MFP after receiving data to verify eligibility.

While we appreciate CMS' clarity on options for providing access to the MFP, PhRMA has significant concerns that the resulting process will add burden to all stakeholders in the pharmaceutical supply chain, significantly increase risks to program integrity, and ultimately impact the Agency's ability to implement the IRA in a successful and orderly manner unless CMS: (1) ensures manufacturers receive data needed to verify MFP eligibility and 340B drug status; (2) removes the requirement for manufacturers to reimburse intermediate entities

[60] CMS. (2023). CMS Drug Spending Dashboards and the Inflation Reduction Act. Available at: https://www.cms.gov/blog/cms-drug-spending-dashboards-and-inflation-reduction-act.
[61] SSA § 1860D-2(d)(1)(D) (as amended by IRA 11001(b)) (Part D negotiated price for a selected drug must be less than or equal to the MFP plus a dispensing fee).
[62] Guidance, p. 31.
[63] Guidance, p. 32.

within 14 days; and (3) uses a more widely available pricing benchmark to define the MFP discount amount. PhRMA strongly urges the Agency to work towards a solution (clarified in guidance), that would:

- ***Provide manufacturers with access to certain data fields from the Part D Prescription Drug Event (PDE) records that will enable manufacturers to verify that a patient is an MFP-eligible individual***. The statute does not require a manufacturer to provide access to the MFP for an individual who is not an "MFP-eligible individual"[64] and therefore, data need to be available to a manufacturer to verify an individual's eligibility for the MFP prior to payment. Similarly, a manufacturer will need appropriate data to provide 340B covered entities (CEs) with the lesser of the MFP and 340B ceiling price, as well as to prevent payment of both an MFP statutory discount and a 340B discount on the same unit as is expressly prohibited under the MFP/340B nonduplication clause.[65] Without access to data for verification, we believe there could be significant disruptions to the Agency's implementation of the IRA, and a significant risk of non-MFP eligible individuals receiving access to the MFP in contradiction to the statute. CMS should expressly acknowledge that manufacturers will establish, receive, review, and as necessary, audit MFP validation data to ensure manufacturers have provided MFP access in accordance with the statute. A list of the minimum needed data fields is included as Exhibit A to this comment letter.

- ***Remove the requirement for manufacturers to reimburse applicable intermediate entities within 14 days for manufacturers choosing a retrospective approach to providing access to the MFP.*** To meet the required payment deadline to pharmacies and other dispensers (hereafter referred to jointly as pharmacies), manufacturers could contract with intermediate entities to facilitate payments to pharmacies in a timely manner, provided those intermediate entities are given access to claims-level transaction data. However, manufacturers need more time than the 14 days proposed by CMS to review claims and verify patient eligibility for the MFP. PhRMA strongly recommends that CMS eliminate the requirement to reimburse intermediate entities within 14 days and instead provide flexibility for intermediate entities and manufacturers to develop processes and set contractual terms related to timing of payment.

- ***Utilize a widely available pricing benchmark such as Wholesale Acquisition Cost (WAC) to define the amount of MFP discounts.*** Acquisition cost is an inappropriate metric to use for defining the amount of MFP discounts. It is currently known solely at the prescription level by the dispensing pharmacy and requiring pharmacies to report the acquisition cost to other stakeholders in the supply chain – who could be playing key coordinating roles in facilitating payment of MFP discounts – could harm competitive incentives in the pharmaceutical supply chain.

PhRMA urges the Agency to improve effectuation of the MFP and minimize stakeholder burden by designating a third-party administrator (TPA) to facilitate this process for manufacturers choosing a retrospective approach. This will best ensure consistent patient access to the MFP at the point-of-sale, enable full reimbursement to pharmacies through a standardized process within the 14-day time frame proposed by CMS, protect program integrity, promote efficiency and accuracy, and minimize stakeholder burden.

If CMS believes it is unable to modify the Guidance to address the three issues noted above, PhRMA strongly urges CMS to withdraw section 40.4 from the revised Guidance. The Agency should instead continue to work with stakeholders to address these issues to meet the needs of all entities within the pharmaceutical supply chain.

PhRMA's additional feedback on this section of the Guidance follows below.

[64] SSA § 1191(c)(2) and section 80 of the Guidance.
[65] SSA § 1193(d)

CMS Needs to Provide Manufacturers with Access to Claims Data for Verification

With or without designating a TPA, CMS must, at a minimum, articulate a process by which manufacturers will receive access to detailed claims data necessary to verify claims, regardless of whether the manufacturer chooses to make the MFP discount available upfront or on a retrospective basis. Manufacturer access to these data is imperative for protecting program integrity. A list of minimum data fields is included as Exhibit A to this letter, and we recommend that CMS seek stakeholder feedback before finalizing this list of data fields.

PhRMA believes it is important for CMS to make these data available to manufacturers, and to do so in an easily accessible format. Manufacturers cannot rely on entering into private contracts with other supply chain stakeholders to secure the data necessary for verification, as these stakeholders may not have access to all required claims-level data elements. For example, if a manufacturer were to contract with a wholesaler to provide pharmacies with access to the MFP, the wholesaler may not have access to the claims-level detail needed for manufacturer verification without significant changes to the existing chargeback system or intervention from CMS.

The Agency's Example of Effectuating the MFP in Section 90.2 of the Guidance is Missing Critical Information Flows Needed to Verify Claims

In section 90.2 of the Guidance ("Monitoring Access to the MFP"), CMS provides an example of how private sector stakeholders could leverage existing systems for manufacturers to provide access to the MFP. Specifically, CMS details a chargeback from a wholesaler to a manufacturer for a retrospective MFP discount to a pharmacy.

Several elements of this example – in which wholesalers would invoice manufacturers for retrospective MFP discount chargebacks – are incompatible with the existing pharmaceutical supply chain infrastructure. First, the MFP must be made available on individual claims, but wholesalers do not currently engage in claims-level data transactions with pharmacies. Either pharmacies would need to begin reporting claims-level data to wholesalers, a burdensome reporting requirement that pharmacies may have significant reservations about undertaking, or wholesalers would need to be given access to portions of PDE data to obtain claims-level data necessary to correctly bill manufacturers for chargebacks.

Second, the Agency's description in section 90.2 describes two "existing mechanisms" to ensure dispensing entities have access to the MFP and to verify that the MFP is only received by MFP-eligible individuals. However, the two mechanisms described by CMS – the RxBIN and Part D processor control number (RxPCN) – are not sufficient pieces of information for a manufacturer to fully verify eligibility for the MFP. For example, it would not be possible from just the RxPCN and RxBIN to identify which medicine is being dispensed, or to confirm that a transaction was not a duplicate or was not later reversed or revised. As noted above, Exhibit A to this comment letter includes a list of minimum fields that are needed for manufacturers to accurately verify eligibility of claims for MFP discounts, and to accurately identify claims subject to 340B discounts.[66] Most of these fields already appear on the Part D PDE record (and many are already provided to manufacturers under the Coverage Gap Discount Program), thus minimizing the reporting burden. PhRMA recommends that the Agency periodically reevaluate data elements necessary to verify MFP eligibility, with industry input, to help minimize operational shortcomings.

The Agency's Proposed Requirement for Manufacturers to Ensure Full Reimbursement to Dispensers and Intermediate Entities, as Applicable, is Not Possible as Drafted within 14 Days

[66] Accurate identification of claims subject to 340B agreements is necessary to ensure manufacturers provide 340B CEs access to the lesser of the MFP or 340B ceiling price.

PhRMA has significant concerns with the Agency's proposed requirement for manufacturers to reimburse any intermediate entities involved in effectuating the MFP within 14 days.

Under the Coverage Gap Discount Program (CGDP), Part D plans (or pharmacy benefit managers (PBMs) acting on their behalf) pay coverage gap discounts on behalf of manufacturers at the time of pharmacy adjudication (which, under prompt pay requirements, occurs within 14 days). But a key reason this system is possible is that manufacturer verification of coverage gap discount claims is permitted on a quarterly basis, some time after the 14-day timeframe for payment to the pharmacy.

PhRMA appreciates the need for timely reimbursement to pharmacies, but we strongly urge CMS to strike the language that would require reimbursement to intermediate entities within the same 14-day window as the pharmacy.[67] This would enable manufacturers to contract with intermediate entities for more time to perform claims verification after pharmacies have been fully reimbursed, as PhRMA does not believe that proper claims verification is possible within the 14-day window. Under the CGDP, for example, manufacturers have 38 days from receipt of an invoice from the CGDP TPA, Palmetto, to pay coverage gap discount obligations. The same 38-day payment window from receipt of invoice also applies to manufacturer rebate obligations under the Medicaid Drug Rebate Program. Indeed, under the Part D program today, plans submit PDE entries to CMS on a two-week cycle. So, CMS itself would barely receive data necessary for verification within the 14-day reimbursement window, let alone have time to make those data accessible to manufacturers for verification.

Acquisition Cost is an Inappropriate Metric to Define the Amount of an MFP Discount

In section 40.4 of the Guidance, CMS proposes that Primary Manufacturers choosing to provide access to the MFP through retrospective reimbursement will need to provide the pharmacy with a discount equal to the difference between the pharmacy's acquisition cost and the MFP.

PhRMA has significant concerns with the Agency's proposal. Acquisition cost is an inappropriate metric for several reasons, including: (1) the dispensing pharmacy's true acquisition cost for an individual prescription is currently unknown to entities outside of the pharmacy; and (2) reporting of the acquisition cost could harm competitive incentives in the pharmaceutical supply chain. Instead, PhRMA urges CMS to exercise its authority under section 1196 of the SSA and define a retrospective MFP discount based on a widely available pricing benchmark like WAC. Specifically, section 1191(a)(4) directs the Secretary to "carry out the…administrative duties…in accordance with section…1196," which, in turn, provides for "[t]he establishment of procedures to carry out the provisions of [the Medicare Drug Price Negotiation Program], as applicable, with respect to [MFP-eligible individuals]."

Pharmacies may purchase medicines from multiple wholesalers at different prices, and the quantity purchased can vary significantly. Individual prescriptions are often comprised of a quantity of medicine pulled from larger bottles received from wholesalers and can even be comprised of a quantity taken from bottles purchased from different wholesalers at different prices depending on the available inventory at the pharmacy. Because of this, only the dispensing pharmacy would be in a position to know the true acquisition cost for a prescription dispensed to an MFP-eligible beneficiary. Wholesalers or other supply chain stakeholders do not currently have insight into the acquisition cost at the prescription level, nor do manufacturers since they typically do not sell medicines directly to pharmacies.

Furthermore, requiring pharmacies to report the acquisition cost for each prescription to intermediate entities for purposes of MFP effectuation has the potential to harm competitive incentives in the pharmaceutical supply chain. For example, if pharmacies are required to include acquisition cost data as part of the claim transaction, this could create incentives for Part D plans and PBMs to limit reimbursement to no more than the reported acquisition cost

[67] The IRA is silent on providing access to the MFP to intermediate entities.

or to limit participation in preferred networks to pharmacies willing to accept cost-based reimbursement. PBMs could also use information about a pharmacy's acquisition cost to cut reimbursement for the pharmacy's non-Medicare patients. Such actions would significantly disadvantage community pharmacies. Additionally, because pharmacies may purchase the same medicine from multiple wholesalers, requiring pharmacies to report acquisition costs to wholesalers could also undermine competitive incentives between wholesaler competitors.

Given the issues with acquisition cost detailed above, PhRMA strongly urges CMS to instead define the retrospective MFP discount based on WAC. Using WAC as the pricing benchmark would reduce the risk of creating misaligned incentives for pharmacies and other stakeholders, and any intermediate entity assisting manufacturers in providing access to the MFP would be able to readily determine WAC on the date of dispense, allowing for a seamless, easy calculation of a retrospective MFP discount amount. On average, WAC tends to be a little higher than pharmacy acquisition costs for brand drugs today,[68] and as such, would best ensure that pharmacies do not incur a shortfall after receiving retrospective reimbursement of an MFP discount and would still allow pharmacies to earn a margin on prescriptions for selected drugs. In contrast, use of acquisition cost, including the National Average Drug Acquisition Cost (NADAC), as a pricing benchmark could significantly reduce or eliminate margins for pharmacies on prescriptions for selected drugs, which could put community pharmacies in particular at risk of closure.

g. Nonduplication with 340B Ceiling Prices (Section 40.4.1)

In section 40.4.1 of the Guidance, CMS states that a Primary Manufacturer is required to provide access to the MFP to 340B CEs if the MFP is below the 340B ceiling price for a selected drug when the CE (or a pharmacy on its behalf, in appropriate cases) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. CMS further states that if the 340B ceiling price is "subsequently determined" to be below the MFP, then the manufacturer is responsible for providing the 340B CE the difference between the MFP and 340B ceiling price.

PhRMA has significant concerns that these proposed requirements do not describe the statutory nonduplication clause correctly and conflict with the Agency's proposal in section 40.4 of the Guidance for manufacturers to provide access to the MFP under a retrospective approach by reimbursing pharmacies the difference between the acquisition cost and MFP within 14 days. Specifically, we believe that the Agency's proposed requirements in each section will result in manufacturers providing duplicate MFP and 340B discounts instead of preventing them.

Currently, we understand many CEs manage their 340B inventory virtually using a replenishment model. Under this model, a 340B CE will track, typically with a computerized system, units of medicines dispensed to 340B-eligible patients. When a certain threshold of units is reached, the CE places an order to replenish that stock at the 340B discounted price.[69] Thus, the medicine is received upfront at the 340B price. This model introduces complexity and is not statutorily mandated.

In such replenishment models, drugs subject to an agreement under section 340B of the Public Health Service Act (340B agreement) are identified after the drug is dispensed. This lag in identification of claims potentially eligible for 340B pricing would make it more difficult to clearly identify whether a 340B discount or MFP discount is owed on a given claim. In addition, it also appears to create an incompatibility with the Agency's proposed requirement for manufacturers to provide pharmacies access to the MFP through a retrospective

[68] Average pharmacy acquisition costs tend to be 4 percent below WAC based on NADAC data. *See* Myers and Stauffer. (2022). NADAC Equivalency Metrics. Available at: https://www.medicaid.gov/medicaid/prescription-drugs/downloads/retail-price-survey/nadac-equiv-metrics.pdf.

[69] For an overview of the physical inventory model and the replenishment model, as utilized by contract pharmacies in the 340B program, please see: OIG. Memorandum Report: Contract Pharmacy Arrangements in the 340B Program. February 4, 2014. Available at: https://oig.hhs.gov/oei/reports/oei-05-13-00431.pdf.

discount equal to the difference between the acquisition cost and the MFP within 14 days, since under the replenishment model, the acquisition cost will vary based on the 340B status of the claim and is not known at the time of dispensing. In other words, a 340B pharmacy using a replenishment model would not know the appropriate acquisition cost in time for manufacturers to meet the proposed 14-day reimbursement requirement. If the pharmacy uses an acquisition cost that is not the 340B price to invoice a manufacturer for a prescription that is later determined to be subject to a 340B agreement, this could result in the manufacturer paying duplicate discounts. And, as noted above, under the IRA's nonduplication clause,[70] a manufacturer owes nothing further to a CE if the CE already acquired the drug at a 340B ceiling price *lower than* the MFP; it only owes the differential between the 340B ceiling price and the MFP if the CE already acquired the drug at a 340B ceiling price that *exceeds* the MFP.

PhRMA urges CMS, in coordination with the Health Resources and Services Administration (HRSA) to issue clear rules for relevant stakeholders to address this conflict and to prevent duplicate MFP and 340B discounts as required under the IRA. PhRMA recommends the Agency consider several potential solutions:

- *Require identification of 340B units at the point-of-sale*. CMS should require identification of 340B units at the point-of-sale through the use of a claims indicator. This would designate the appropriate acquisition cost, as the 340B status of each prescription would immediately be known and allow manufacturers to be able to pay the retrospective discount to the pharmacy upon appropriate verification from the CE within 14 days.[71] The use of a claims indicator would also align with the requirement for CMS to identify and exclude 340B units from the Part D inflation rebate beginning in 2026.

- *Clarify that manufacturers can choose to make the MFP the "default payment*." In coordination with HRSA, CMS could require CEs to follow a new retrospective discount mechanism (i.e., a "rebate") to obtain 340B pricing for selected drugs. CMS should revise the Guidance to state that manufacturers could initially provide the MFP to CEs (or pharmacies dispensing medicines on their behalf) for verified MFP-eligible individuals and then later reimburse CEs for any difference owed between the MFP and the 340B ceiling price (if lower) as a rebate. Under this approach, when invoicing manufacturers, pharmacies or a coordinating intermediate entity would then always use a non-340B acquisition cost for an MFP drug to determine the retrospective MFP discount amount. If it was determined later that a drug was subject to a 340B agreement, and the 340B ceiling price was below the MFP, a manufacturer would reimburse the CE for the difference between the MFP and 340B ceiling price after receiving an invoice from the CE.[72]

If CMS is not able to address the inconsistency between the proposed Guidance in sections 40.4 and 40.4.1 using one of the solutions outlined above, or another approach, PhRMA urges CMS to withdraw sections 40.4 and 40.4.1 from the revised Guidance to avoid confusion. This would give the Agency additional time to develop a replacement solution to the complicated intersection between 340B and the MFP that works for stakeholders and adheres to the statute's nonduplication clause.

Identifying Units Subject to 340B Agreements

Regardless of the approach CMS chooses to adopt to reconcile the inconsistency between sections 40.4 and 40.4.1 of the Guidance, the accurate identification of units of selected drugs subject to 340B agreements is critical to allowing manufacturers to meet their obligation to provide CEs with the lesser of the MFP or 340B ceiling price

[70] SSA § 1193(d).
[71] Ibid.
[72] This proposal should be read consistent with PhRMA's position on the 14-day requirement for providing access to the MFP, as set forth in the preceding section of this comment letter.

when the CE (or a pharmacy on its behalf, in appropriate cases) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. Without an accurate way to identify 340B units, manufacturers could be at risk of paying multiple discounts that are meant to be prevented by law.

PhRMA continues to support the Agency's proposal in the Part D inflation rebate Guidance to require a 340B indicator be included on the PDE record and on all pharmacy claims.[73] PhRMA also urges CMS to add a second, "non-340B" indicator value such that the PDE is never silent on the 340B status of each claim. PDE submissions without either of the two indicator values should be rejected as incomplete. This approach would give CMS needed certainty that a 340B determination has been made for each claim. In addition, this would align with the approach taken by the Agency for the discarded drug refund modifier, where providers and suppliers submitting claims for single-dose container or single-use package drugs under Part B must use the "JW" modifier to indicate the amount of a medicine that was discarded, or, effective July 1st, 2023, use the "JZ" modifier to attest that no amount of a medicine was discarded.[74]

Even with a set of mandatory claims indicators, however, PhRMA has significant concerns that all prescriptions subject to a 340B agreement may not be appropriately captured, which could undermine the ability of manufacturers to meet their obligation to provide CEs with the lesser of the MFP or 340B ceiling price when the CE (or a pharmacy on its behalf) dispenses a selected drug to a 340B patient of the CE who is also a Medicare beneficiary. A recent report by IQVIA found that only 61 percent of treatments for Part B separately payable drugs originating at rural referral centers and sole community hospitals used a relevant 340B modifier,[75] a highly concerning result given that CMS requires these entities to use the "JG" and "TB" modifiers on claims seeking Medicare payment for a 340B-acquired drug. By comparison, IQVIA found that 89 percent of treatments for Part B separately payable drugs originating at disproportionate share hospitals (DSHs) used a relevant modifier.[76] Since the requirement to use either the "JG" or "TB" modifiers applies equally to DSHs, rural referral centers, and sole community hospitals, the reasons for the significantly different rates of modifier use are unclear.

PhRMA believes that the addition of a "non-340B" indicator value and the rejection of PDE records that lack one of the two relevant values discussed above will help to improve appropriate reporting of units subject to 340B agreements. PhRMA further encourages CMS to establish a robust process to audit 340B CEs to confirm the appropriate identification of units subject to 340B agreements, with penalties for CEs found to be out of compliance. Alternatively, CMS could establish a clearinghouse-type organization to identify 340B units dispensed or administered to Medicare enrollees. The 340B clearinghouse would act as a claims verifier, reviewing Part D PDE data as well as data submitted by 340B CEs (or entities acting on their behalf) to confirm whether a claim is subject to a 340B agreement, similar to the role played by 340B TPAs and split-billing vendors today.[77] Part D claims identified as being subject to a 340B agreement by either claims indicators or the clearinghouse would then be shared with manufacturers.

Without either a mandate to use a 340B indicator on the PDE or a data clearinghouse that can share identified 340B claims with manufacturers, it is unclear which mechanism manufacturers could use to provide CEs with the lesser of the MFP or 340B ceiling price when a selected drug is dispensed to a 340B patient of the CE who is also

[73] CMS. (2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of SSA, and Solicitation of Comments. Available at: https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf

[74] CMS. (2023). Discarded Drugs and Biologicals – JW Modifier and JZ Modifier Policy: Frequently Asked Questions. Available at: https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatientpps/downloads/jw-modifier-faqs.pdf

[75] IQVIA. (2023). Can 340B Modifiers Avoid Duplicate Discounts in the IRA? Available at: https://www.iqvia.com/-/media/iqvia/pdfs/us/white-paper/2023/can-340b-modifiers-avoid-duplicate-discounts-in-the-ira.pdf.

[76] Ibid.

[77] 340B TPAs and split-billing vendors assist 340B CEs in managing prescription 340B eligibility, ordering, and payment. These entities track electronic data feeds (such as inpatient or outpatient status, prescriber eligibility, clinic location, Medicaid payor status, drug identifier, and quantity dispensed) to assess 340B patient eligibility.

a Medicare beneficiary. Thus, it is imperative for CMS to adopt an approach to accurately identify all Part D prescriptions subject to 340B agreements.

II. Negotiation Factors (Section 50)

Sections 50 and 60 of the Guidance describe numerous, closely related elements of the MFP price-setting process (statutory factors, price setting methodology and process, respectively). Overall, CMS' approach to defining the statutory factors in section 50 and Appendix C, as well as the process and methodology described in section 60, falls short of establishing a "consistent process and methodology" for MFP price setting as required in section 1194 of the SSA. To be truly consistent, a methodology must provide a reasonable degree of predictability for stakeholders – particularly manufacturers – on how the factors, and data that underpins them, affect the outcome of the Agency's decision.

Unfortunately, the initial guidance falls short of these standards. The lack of specificity in how individual factors are defined and weighted, combined with an opaque process, results in a subjective and arbitrary price setting framework. We urge CMS to make changes in a revised Guidance to provide needed clarity and specificity in the MFP methodology and factor definition, without resorting to a formulaic approach that does not allow the needed flexibility to account for important clinical differences between medicines and therapeutic areas.

Despite the lack of specificity in the proposed methodology and factor definition, the few details that CMS does articulate almost uniformly point to an approach that will significantly exacerbate the underlying flaws in the statute itself and worsen the impact on patients. Because the IRA directs CMS to "consider" a host of factors, the Agency could balance the factors in a manner that rewards innovation, preserves patient care and advancement, and ensures manufacturers – at a minimum – recoup R&D and costs of production and distribution. Instead, the Agency proposes to:

- Define factors in ways that seem explicitly designed to drive the MFP to excessively low "cost-plus" pricing levels;
- Propose an approach to calculating R&D cost "recoupment" that doubles down on the inherent flaws in the statute's unprecedented inclusion of the concept; and
- Penalize rather than reward manufacturer investments in continued R&D following a drug's approval.

Together, these choices strongly suggest a predisposition to devalue the factors related to the clinical benefits and value of medicines to patients which could help mitigate the law's adverse impact on medical progress. We elaborate on our concerns with CMS' proposed definitions of the statutory factors below. In section III, we discuss concerns with CMS' methodology and process for setting MFPs.

a. Requirements for Submission of Manufacturer Submitted Data Generally (Section 50.1)

In section 50.1 of the Guidance, implementing the "manufacturer-specific data" provisions of IRA (SSA 1194(e)(1)), CMS states that it intends to require that a Primary Manufacturer submit data related to the selected drug to CMS regarding R&D costs of the Primary Manufacturer and whether the Primary Manufacturer has recouped those costs; current unit costs of production and distribution; prior federal financial support for the drug's discovery and development; data on pending and approved patent applications, patent exclusivities, and NDA/BLA approvals; and market data and revenue and sales volume data in the U.S. for the Primary and Secondary Manufacturer. Appendix C of the Guidance includes a list of definitions that describe the data to be collected for the Program.

CMS intends for the Primary Manufacturer to aggregate data from both the Primary Manufacturer and Secondary Manufacturer on the non-FAMP, current unit costs of production and distribution, market data, and revenue and sales volume. It is not workable for Primary Manufacturers to report these data on behalf of Secondary

Manufacturers since Primary Manufacturers likely lack access to such data from Secondary Manufacturers, either legally or practically. See section I, subsection (a) of our comments for our detailed concerns with this part of the Guidance. In addition, as discussed above, there is insufficient time to modify contracts between the parties prior to October 1st, 2023. Further, even if these data were only being collected and submitted by the Primary Manufacturers, we are concerned that the proposed data will be virtually impossible for manufacturers to collect and submit within the 30-day timetable envisioned by the Agency. ***CMS has discretion under the law to permit additional data submission after the October 2nd, 2023 deadline, and we strongly recommend the Agency exercise this discretion.***

Because much of the data required by the IRA are already provided by biopharmaceutical companies under other statutory requirements, CMS should obtain relevant data from publicly available sources wherever possible. For example, ***PhRMA recommends that CMS obtain information about approved patent applications from the FDA's Orange and Purple Book listings and information about approved applications from Drugs@FDA, rather than impose additional burden on manufacturers to submit these data, and companies should be explicitly permitted to reference such sources in their submissions to CMS***. ***Conversely, manufacturers should be permitted to voluntarily provide additional data about manufacturer-specific factors, which could provide necessary context or be helpful to CMS, at their discretion, due to the varied ways in which manufacturers record and maintain information about these factors***. We note that several areas of the Information Collection Request (ICR) form lack sufficient text limits to allow companies to provide adequate supporting information when companies deem it would be helpful to inform CMS decision-making and should not be constrained in their ability to provide such information. ***PhRMA recommends that CMS amend the Guidance to allow sufficient space for manufacturers to provide a rationale for calculations that approximate spending on manufacturer-specific data elements or have referenced other publicly available information where necessary.***

b. Research and Development (R&D) Costs (Appendix C)

While the statute directs CMS to "consider" R&D costs and the extent to which the manufacturer has recouped such costs, nowhere does the IRA require penalizing biopharmaceutical innovators for recouping R&D, as CMS appears to propose. Indeed, as noted above, the factor could just as easily be read to require a floor, ensuring that, at a minimum, a manufacturer be permitted to recoup R&D. Unfortunately, CMS has chosen to establish standards for the R&D factor that are untethered from the realities of how biopharmaceutical progress occurs, failing to reflect or account for the high-risk nature of research and drug discovery and the complex ecosystem underpinning the U.S. biopharmaceutical research and development enterprise.

CMS also defines the factor in an overly narrow manner, stating that it will review a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug, such as basic pre-clinical research costs, post-Investigational New Drug (IND) application costs, FDA Phase IV clinical trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. CMS proposes to calculate "recoupment" of R&D costs by comparing them to global, total lifetime net revenue for the selected drug. CMS would then increase or decrease the preliminary MFP it calculates depending on whether costs have been "recouped."

CMS' proposal to deem that a manufacturer has "recouped" investment based on the global net revenue for the product is fundamentally at odds with maintaining strong incentives for continued R&D. Currently, the biopharmaceutical industry is acknowledged by the Congressional Budget Office (CBO) to be one of the most R&D-intensive in the U.S.[80] In 2020, U.S. biopharmaceutical R&D investment totaled $122 billion.[81] Companies invest on average over 20 percent of revenue in R&D,[82] and in total account for approximately 18 percent of all business-funded R&D in the country, according to data from the National Science Foundation.[83] The Brookings Institution reported in 2015 that in 2009 the pharmaceuticals and medicines sector had the highest R&D spending per worker among 50 R&D- and STEM knowledge-intensive industries, at $143,110. The sector coming in

second on this measure, communications equipment, was more than $50,000 lower per worker. Even a cutting-edge, high investment sector like semiconductors and other electrical components had R&D spending of only $49,612.[78] In sum, the biopharmaceutical industry is the United States' most R&D-intensive sector.

The Agency's flawed approach to assessing "recoupment" of costs reflects a misunderstanding of the economics of the global biopharmaceutical marketplace. Only one of thousands of potential candidates will ultimately result in an FDA-approved medicine, and less than 12 percent of the candidate medicines that make it into Phase I clinical trials are ultimately approved by the FDA.[76] Following approval, many medicines face significant competition or are not a commercial success.[77] [78] Companies account for these odds when they plan their R&D programs. The revenues from a few successful medicines support continued investment in the high-risk effort to discover new medicines and help to recoup costs of the many failures across their entire portfolio of medicines, not simply, as CMS proposes, those in the same therapeutic class or with the same intended mechanism of action. In sum, because selected drugs are among the subset of medicines with the highest spending in Medicare, they are *by definition* successful and thus likely to have "recouped" their R&D costs by CMS' definition, especially when defined as narrowly as CMS has proposed.

Based on section 60.3.4, CMS appears to be planning to compare global net revenue to R&D costs as defined by CMS to determine whether a manufacturer has recouped its R&D costs. Nowhere does CMS acknowledge that manufacturers necessarily incur a wide range of expenditures, beyond R&D. For instance, manufacturers also must manufacture a drug, incur expenditures to sell a drug in order to earn revenue on it, pay taxes, operate compliance programs, and engage in a variety of other costly operations. Without performing these core functions, a manufacturer would not be in a position to perform R&D. Therefore, CMS' narrow definition greatly overstates revenue that, even in its flawed construct, can reasonably be counted as "recouping" R&D costs.

CMS' definition also ignores ex-U.S. costs necessary to generate global sales. Over the last 20 years the use of multi-regional clinical trials (MRCTs) has become a preferred strategy for rapid new drug development.[79] MRCTs are conducted in more than one region under a single protocol and allow data generated in one country or region to be leveraged to help gain approval in another country or region. These studies, in addition to clinical trials that may be conducted solely outside the U.S. at the request of regulators, are required for achieving sales in countries around the world and are not necessarily costs related to the U.S. regulatory requirements for INDs or NDA/BLAs. Despite requiring manufacturers to provide the global, total lifetime net revenue from global product sales, CMS' methodology does not explicitly account for these ex-U.S. costs – further increasing the likelihood that manufacturers will be penalized for having "recouped" their costs under CMS' skewed methodology.

All of these concerns reflect the fallacy of CMS' unnecessary interpretation of the IRA, as well as its definitions of costs and "recoupment," both of which will arbitrarily and unnecessarily shift the price down. Given the discretion of the statute (to consider R&D recoupment as a floor, not a downward adjustment), the fact that such downward adjustments could never result in a "fair price," and the economic model that fuels medical advances, CMS should, in specifying "how or to what degree" this factor is applied, state that it will not be used to lower a price determined on the basis of a drug's therapeutic and clinical attributes.

PhRMA recommends that to the extent CMS maintains the flawed proposal on "recoupment," it should place minimal weight on this factor and specify that it will not be used to reduce an MFP determined on the basis of a drug's therapeutic and clinical attributes. Furthermore, the Agency should count only a fraction of global net revenue toward "recoupment" of R&D costs.

[78] Muro, M., Rothwell J., Andes S., Fikri K., Kulkarni S. (2015). America's Advanced Industries. Brookings Institute. Available at: https://www.brookings.edu/wp-content/uploads/2015/02/AdvancedIndustry_FinalFeb2lores-1.pdf.

Finally, CMS' approach to implementing this aspect of the statute is not only at odds with the way that manufacturers operate and invest in R&D, but also creates significant burden and complexity. In most cases it will be extremely challenging for manufacturers to quantify costs as required by CMS – and will be virtually impossible to comply within the 30-day timeframe. CMS has requested that manufacturers provide the costs of direct and indirect basic pre-clinical research costs on drugs with the same active moiety/active ingredient or mechanism of action as the selected drug that did not make it to clinical trials. This will require companies to produce a record of costs incurred for pre-clinical data that may be 20 or more years old, a herculean task. For companies with ex-U.S. headquarters, global data may not be easily accessible, or accessible at all, in the normal course of business to U.S. affiliates. In addition, pre-clinical costs may include, for example, investments in platform technologies that are used across multiple drug development programs, as well as development tools such as model-informed drug development or AI programs. As a result, calculation of product-specific R&D will require allocation of costs across drug development programs and products at the level of granularity which is prescribed in the guidance. Similarly, costs for "abandoned and failed" products may be difficult if not impossible to attribute to a drug development program in the ways CMS has specified. These difficulties are compounded when drug products are developed through the efforts of multiple companies, through early-stage R&D licensing arrangements, or other partnerships.

We urge CMS to recognize total investments across the entire portfolio. Rather than creating requirements that are virtually impossible for companies to accurately comply with, CMS should provide manufacturers with flexibility to provide information on broader R&D costs, including information about pre-clinical costs, failed and abandoned drug costs as well as "other R&D costs." Other costs may include costs of global development and regulatory submission activities. Companies should also be permitted to rely on benchmark/industry-wide data in cases where a company may not maintain the data itself.

CMS should amend the Guidance to limit required submission of R&D costs to data available to the manufacturer that can be directly attributable to the selected drug, while allowing companies to voluntarily provide supplemental data. In addition, manufacturers should be given the opportunity to provide a supporting narrative.

c. Current Unit Costs of Production and Distribution (Appendix C)

Regarding current unit costs of production and distribution, CMS would define costs of production to include all direct and indirect costs related to purchasing raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals; formulating and preparing the finished drug product; performing quality control and testing of the drug; and operating costs for personnel, facilities, transportation, any importation, and other expenses related to preparing the finished drug product. Distribution costs would include all direct and indirect costs related to packaging and materials; labeling; shipping to any entity that acquires the drug from the Primary or Secondary Manufacturer; and operating costs for any of the above. Current unit costs would include only costs incurred by the Primary and Secondary Manufacturer and only units produced and distributed for sale in the U.S. R&D costs and marketing costs would not be included.

CMS' proposed definition for the unit costs of production and distribution in the Guidance is concerning. CMS has expanded the language on this factor beyond the statute to a level of additional detail and specificity that companies may not have access to, particularly in situations where companies may be working with additional suppliers and manufacturers in the supply chain. ***PhRMA strongly recommends that rather than specifying the definition, CMS allow discretion for manufacturers to describe production and distribution costs which they are able to report and to provide a narrative explanation describing how these costs were calculated.***

d. Prior Federal Financial Support (Appendix C)

CMS would define prior federal financial support to include tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government to support discovery, research, and/or development of the selected drug – all during the time period from when initial research began or when the drug was acquired by the Primary Manufacturer, through the date the most recent NDA/BLA was approved. CMS states that it may consider decreasing the preliminary price if funding for the drug's discovery and development was received with federal financial support.

PhRMA is disappointed with CMS' decision to broadly define federal financial support and strongly disagrees with the notion that tax credits, including orphan drug tax credits, are appropriate for inclusion as "prior federal financial support," which would serve to undermine the incentive that the credits are intended to provide by decreasing a selected drug's MFP. Tax credits serve to incentivize R&D spending on life-saving medicines and, for orphan drugs, that spending is for medicines for rare diseases. These tax credits are critical to incentivize innovation and are not akin to the government providing direct support to a company's research efforts and CMS' policy undermines longstanding intent by Congress to incentivize R&D into these difficult to treat diseases. ***PhRMA urges CMS to remove tax credits from the definition of "prior federal financial support."***

America's biopharmaceutical industry is at the heart of a robust R&D ecosystem that develops more innovative drugs than any other country in the world. The industry's unique role in that ecosystem is to utilize its scientific and industrial expertise to take the necessary risks to build upon and further advance basic science research into safe and effective treatments that can be made available to patients. Private sector companies regularly fund academic researchers and collaborate with government-funded scientists to advance a variety of promising scientific concepts to better understand various disease states and drug targets. However, many of those explorations are not ultimately included in developing the actual products for patient use. Rather, this knowledge must be shared and further expanded upon to contribute to potential new drugs and drug targets. ***Therefore, PhRMA recommends that CMS limit its consideration of prior federal financial support for discovery and development solely to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug (e.g., excluding basic science, research tools, or similar general concepts). PhRMA also requests that CMS clarify that prior federal financial support needs to be reported only for the time period starting when the Primary Manufacturer acquired the drug, even where this approach may result in the reporting of no prior federal financial support during the relevant period for products associated with patent applications that included a government interest statement.***

e. Patents, Exclusivities, and Approvals (Appendix C)

Regarding patents, exclusivities, and approvals, CMS considers relevant patents to be those that are pending or approved and linked to the selected drug as of September 1st, 2023, as well as pending and approved applications for which a claim of patent infringement could reasonably be asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug. CMS notes that FDA exclusivity periods include Orphan Drug Exclusivity and Pediatric Exclusivity. CMS states that it will consider the length of the available patents and exclusivities before the selected drug may no longer be single source and may consider decreasing the preliminary price if the selected drug has patents and exclusivities that will last for a number of years.

PhRMA strongly disagrees with CMS' proposal to decrease the MFP for selected drugs that have remaining patents and exclusivities. Instead, we recommend CMS take the opposite approach and recognize the benefit provided by these investments and consider adjusting the preliminary price upward based on these protections. Patent rights are a form of intellectual property (IP) protection enunciated in the U.S. Constitution and are critical to the continued investment in R&D, including for new medicines and improvements for existing medicines. Patents require the description of inventions to be disclosed to the public, allowing society to understand and learn from the invention, and this disclosure lays the groundwork for competition from nonidentical drugs that treat the

same conditions as well from generics and biosimilars. Annualized savings from biosimilars reached $6.5 billion in 2020, and competition from generics and biosimilars is expected to reduce U.S. brand sales by $128 billion through 2025.[79]

CMS' proposal to penalize manufacturers for the lengthy, costly, and risky R&D that has resulted in new innovations protected by patents and exclusivities will undermine U.S. leadership in biopharmaceutical innovation and weaken the intent of the IP system. As a matter of course, drugs selected for price setting at 7 or 11 years will have remaining patents and exclusivities, which may include, for example, unexpired 7-year orphan-drug exclusivity for an orphan indication approved after the drug's initial approval or a 3-year new clinical exclusivity earned through new clinical trials of a drug product. Indeed, as a matter of law, innovative biologics receive 12 years of exclusivity following first licensure, and pediatric exclusivity would extend this period another six months. Thus, CMS' policy choice of penalizing patents and exclusivities would broadly undercut incentives for progress.

In addition, manufacturers should not be penalized in cases where they have obtained patents and exclusivities for innovation, including for important advances and improvements made after an initial FDA approval. Patents and exclusivities covering post-approval innovations may not affect the timing of approval and launch of generic or biosimilar products that omit a new indication, do not seek approval of an improved formulation, or are not made using a more efficient manufacturing process. It would be unjust to penalize manufacturers for obtaining patents and exclusivities that do not extend the single-source status of a product. Additionally, by choosing to adopt a policy of reducing the MFP from the ceiling price due to the existence of remaining patents and exclusivities, CMS would eviscerate these incentives that Congress created to promote innovation, knowledge-sharing, and benefits to patients and society. For example, existing incentives in the Best Pharmaceuticals for Children Act to conduct pediatric development beyond any required pediatric studies would be weakened. Actions related to patents should be left to legislation and where appropriate, the proper administrative body, i.e., USPTO. There is no indication that Congress intended for the IRA to hollow out these incentives in the manner that CMS proposes. Indeed, by imposing a financial penalty on manufacturers for obtaining patents and exclusivities, CMS would exacerbate the serious concerns that the Program raises under the Takings Clause of the Fifth Amendment to the U.S. Constitution, including by effectively depriving manufacturers of part of the value of a patent or exclusivity.[80]

Post-approval R&D often results in innovations that can improve patients' lives. In fact, more than 60 percent of oncology medicines approved a decade ago received approvals for additional indications in later years, and most of those occurred seven or more years after initial FDA approval. Such post approval research often requires lengthy and costly clinical trials, taking a total of three to six years. Penalizing manufacturers for both patents and/or exclusivities on the original product as well as post-approval innovations would fundamentally change incentives for improving patient and doctor choice as well as continued investment in research following a drug's initial approval. Perversely, CMS' proposed policy would penalize the development of the very attributes of medicines and knowledge about medicines' performance that CMS states it will evaluate under the elements of this Guidance related to assessing a drug on its clinical dimensions. Indeed, the statutory classification of a selected drug as a short-monopoly drug, extended-monopoly drug, or long-monopoly drug already provides a mechanism for reducing the ceiling price and renegotiating the MFP as additional years elapse since approval. CMS should not further penalize manufacturers in the manner described in the guidance. ***PhRMA urges CMS to amend the Guidance and clarify that if a drug has existing unexpired patents or exclusivities, rather than penalizing the manufacturer with a lower price, it should result in an upward shift of the preliminary price to reflect the innovation in the product.***

[79] IQVIA Institute Report (2020). Biosimilars in the United States 2020 – 2024.
[80] U.S. Const., Amend. V.

Regarding submission of information on pending or approved patent applications, ***PhRMA suggests that CMS consult the FDA's Orange and Purple Book listings, as well as provide flexibility for manufacturers to supplement these listings to provide information about pending patent applications and other relevant facts***. CMS should not use information about pending patent applications to adjust its preliminary price downward. Claims for infringement cannot be based on a pending application, and it would be premature to decide about the exclusionary effect of a patent application before issuance of a patent because the claims can change significantly during prosecution and a patent ultimately might not be granted. Also, CMS should explicitly confirm that "pending applications" for submissions purposes do not include abandoned applications, which would not be relevant for CMS' price-setting process and are considered neither pending nor approved patent applications. CMS should further clarify that manufacturers are not required to submit non-public patent information, including information about pending applications that have not been published, given the highly confidential nature of this information. Manufacturers should also be permitted to refer CMS to the Orange and Purple Book for exclusivity data and Drugs@FDA for information about approved applications. Manufacturers could then supplement those sources with information about pending applications.

In addition, the definition of relevant patent information to include pending and approved patent applications "relating to the selected drug" and patents "linked to the selected drug" is vague and could encompass patents and patent applications that have no bearing on the continued single-source status of a selected drug.[81] For example, it could entail the submission of information about foreign patents and patent applications, as well as patents that are neither owned nor licensed by the Primary Manufacturer. The reference to "patents linked to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant," in particular, is inconsistent with the statutory requirement that the manufacturer submit "[d]ata on pending and approved patent applications . . . for the drug."[82] Moreover, it is unclear how the scope of relevant patent information defined in the Guidance aligns with the statutory standard for the listing of patent information in the Orange Book.[83] ***CMS should only consider patents and patent applications that are directly related to the selected drug, as opposed to those directed to basic science, research tools, and similar general concepts, manufacturing processes, unapproved uses, unapproved formulations and dosage forms, metabolites, intermediates, and third-party patents and applications for which the manufacturer has no rights of enforcement***. CMS should only require information about patents and patent applications that is relevant to whether a selected drug will remain single source. CMS should provide a standard for relevance that is consistent with the scope of the requirement to submit patent information for listing in the Orange Book and Purple Book.

f. Market Data and Revenue and Sales Volume Data (Appendix C)

CMS proposes to require that manufacturers report more than 20 metrics relating to drug prices and sales under "Market Data and Revenue and Sales Volume Data" (see Appendix C): WAC unit price; National Council for Prescription Drug Programs (NCPDP) billing unit standards; 340B ceiling price; Medicaid Best Price; AMP; 340B prime vendor program price; Federal supply schedule (FSS) price; Big Four price; U.S. commercial average net unit price, with and without patient assistance and "best"; manufacturer average net unit price to Part D Plan sponsors with and without patient assistance and "best"; total U.S. gross revenue; total U.S. net revenue with and without patient assistance; and quarterly total U.S. unit volume. In most cases CMS would require the Primary Manufacturer to aggregate its own data on the selected drug from both the Primary Manufacturer and data from

[81] Guidance at 88.
[82] SSA § 1194(e)(1)(D).
[83] *See* Federal Food, Drug, and Cosmetic Act § 505(b)(1) (requiring the submission of patent information for "any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug.").

any Secondary Manufacturer. The Guidance specifies that all of these data with explanations must be submitted to CMS within 30 days of selection – by October 2nd, 2023.

PhRMA has major concerns with these reporting requirements specified as "Market Data and Revenue and Sales Volume Data." These requirements are extremely broad and would impose substantial burdens on manufacturers, especially given the short time period to collect the data and the need to gather data from all Secondary Manufacturers. As discussed in response to section 40, it would be legally problematic and extremely challenging for Primary Manufacturers to gather the vast amounts of data CMS is asking them to collect from Secondary Manufacturers. CMS fails to provide any justification or rationale for the breadth of this proposed data requirement. The Guidance also introduces two new pricing metrics (each with three variations) with little explanation as to which sales and discounts should be included in and excluded from these calculations. Manufacturers are required to report a new "U.S. commercial average net unit price" in three ways (with patient assistance programs, without patient assistance programs, and "best" price) and a "manufacturer average net unit price to Part D Plan sponsors" similarly (with patient assistance programs, without patient assistance programs, and "best" price).

CMS unjustifiably fails to define these new metrics with specificity or any reference to existing terms or rules, which is a marked departure from how Congress and agencies have defined pricing metrics and calculations in other federal drug pricing programs such as the Medicaid Drug Rebate Program, the 340B Drug Pricing Program, the Federal Ceiling Price statute and related U.S. Department of Veterans Affairs (VA) guidance, and the FSS. In doing so, CMS fails to grasp the potential for the lack of clear definitions to cause inconsistency in the way these metrics are reported and calculated, and thus what meaning they may have. Without additional CMS guidance, these metrics would pose considerable risk to manufacturers, who will be required to report in a compressed timeframe under the serious threat of CMPs. Moreover, the new reporting requirements, if finalized, would place unnecessary burdens on manufacturers given that a significant portion of this information is already reported to and available to CMS such as net prices to Part D and Medicaid Best Price.

To help address such gaps in reporting instructions, manufacturers would have to develop a set of reasonable assumptions to calculate these various new metrics and then rely on these assumptions to report these metrics. Yet the Guidance increases the risk of nonuniform and perhaps unintentionally inaccurate reporting in multiple ways, including the following:

- The Guidance makes flawed assumptions about manufacturer patient assistance, requiring that manufacturers calculate and report new metrics with and without patient assistance ("U.S. commercial average net unit price," with and without patient assistance; "manufacturer average net unit price to Part D Plan sponsors" with and without patient assistance; and "total U.S. net revenue" with and without patient assistance). Patient assistance is financial assistance intended to reduce patients' out of pocket costs and is not considered a price concession offered to customers.[84] In other words, patient assistance does not constitute "market" data under SSA §1194(e)(1). But this is the rubric under which CMS would require manufacturers of selected drugs to report their patient assistance amounts.

- Moreover, the Guidance would require manufacturers to calculate and report a Part D price ("manufacturer average net unit price to Part D Plan sponsors") "with patient assistance" when the

[84] See, e.g, 42 CFR § 447.505(c)(8)-(12)(CFR as of December 31, 2020) (excluding from Medicaid Best Price specified types of patient assistance, to the extent the benefits were not provided to other parties, regulations that were revised by a December 31, 2020 "accumulator adjustment rule" that was itself overturned in court); *PhRMA v. Becerra*, 2022 WL 1551924, *5 (D.D.C. 2022)(overturning the "accumulator adjustment rule" that would have generally resulted in manufacturers having to include patient assistance in their Best Price determinations, and emphasizing that "A manufacturer's financial assistance to a patient does not qualify as a price made available from a manufacturer to a best-price-eligible purchaser. Rather, a manufacturer's financial assistance is available from the manufacturer to the patient").

federal anti-kickback statute would generally prohibit them from offering cost-sharing assistance to Part D patients, and when patient assistance is not given to or intended for any type of "plan sponsors" – all of which raises further questions and confusion about what CMS even means by "patient assistance" and thus how manufacturers could reasonably interpret and carry out these new reporting mandates.

- A closely related source of confusion and uncertainty – and risk–-- is that the Guidance is silent on whether a "patient assistance program" is meant to include a manufacturer's charitable free drug programs (which it should not). The fact that CMS refers to "patient assistance" in a Part D context where manufacturers do not provide cost-sharing assistance to patients causes further questions about what CMS means by "patient assistance." Yet there is language in the data elements ICR that seems to consider only "coupons and copay assistance" as the patient assistance that CMS is asking manufacturers to report.[85]

To correct these problems, CMS should withdraw all of the new metrics. Failing that, CMS should delete all items asking for manufacturers to report "patient assistance" from the Guidance (and the related data elements ICR). If any references to patient assistance are retained, we ask that CMS define what constitutes a "patient assistance program" and explicitly clarify that a "patient assistance program" does not include manufacturer charitable free drug programs.

It might appear initially that manufacturers of selected drugs could resolve all of these problems by adopting appropriate reasonable assumptions and specifying these assumptions in their data reports to CMS. But manufacturers are being required to develop their reasonable assumptions, perform and test their calculations, and report this information to CMS – in some cases all while collecting and seemingly blending in data from one or more Secondary Manufacturers, plus with caps on the amount of text they can provide in their narratives explaining their reported data to CMS – in a time frame that is impracticable, and at risk of severe penalties for submitting data that CMS ultimately deems insufficient or inaccurate.[86] These burdensome procedures are in no way necessary for CMS to make MFP determinations and accordingly we urge CMS to rectify these problems when revising its Guidance.

Finally, PhRMA takes issue with how CMS plans to use the market and sales data during the price setting process. For example, according to section 60.3.4 of the Guidance, if one of the new metrics reported – e.g., "average commercial net price – is lower than the "preliminary price," CMS may adjust the preliminary price downward. Yet CMS provides no explanation for the relationship between these prices, or for why a lower commercial net price (or any of these pricing metrics) should drive the preliminary price down, and likely result in a lower MFP.[87]

CMS should at a minimum withdraw these new metrics (i.e., all three variations of "U.S. commercial average net unit price" and "manufacturer average net unit price to Part D plan sponsors, respectively) in the revised Guidance. In the revised Guidance CMS should only require reporting of existing price reporting metrics (e.g., WAC, AMP). It is also critical that CMS permit manufacturers to submit all of the market and sales data under a reasonable timeframe (and in particular beyond October 2nd, 2023, which we believe the statute permits), and without limits on the number of lines or words manufacturers can use to explain their assumptions or other aspects of their metrics.

[85] ICR for Negotiation Data Elements under sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW) Questions 31-36, p. 33-37.
[86] Id. The ICR limits manufacturer responses explaining their reported pricing data and reasonable assumptions to a free text box that has a "1,000 word limit." P. 35-36.
[87] Guidance, p. 53.

g. Quality-Adjusted Life Years (QALY) and Cost Effectiveness Analysis (Section 50.2)

PhRMA appreciates CMS' acknowledgement that it will not use quality-adjusted life years, or QALYs, in its determination of MFPs for selected drugs in a "life-extension context," given their discriminatory nature and failure to accurately capture the benefits treatments offer to patients. (CMS does not define "life extension context" in the Guidance document.) While we agree with CMS' statement that the language set forth in the IRA prohibits CMS' reliance on QALYs or similar metrics, we are concerned that CMS overlooks a separate, but equally relevant prohibition on reliance on QALYs that is more broadly applicable across Medicare that was enacted as part of the Affordable Care Act.

Specifically, CMS fails to reference the existing prohibition on Medicare reliance on QALYs or similar metrics found in in the SSA.[88] This prohibition would prevent CMS from using QALYs as part of its determination of MFPs, including a in a "life extension context", including in CMS' determinations of MFPs. ***PhRMA recommends CMS explicitly acknowledge this additional statutory prohibition in its revised Guidance, and refrain from using QALYs or any similar metric, in any context.*** Given the concerns of numerous stakeholders regarding use of QALYs and similar metrics, clarity and transparency in this matter is absolutely critical as CMS implements the Program. By clearly and unequivocally precluding these standards from MFP decision-making, CMS will build trust with stakeholders and the public at large.

It is widely acknowledged that QALYs, which are the basis for many cost effectiveness analyses (CEA), discriminate against seniors, the disabled, communities of color, and the chronically ill. As noted by the National Council on Disability, "QALYs place a lower value on treatments which extend the lives of people with chronic illnesses and disabilities."[89] These concerns have been echoed repeatedly by numerous stakeholders – in 2021, more than 80 stakeholder groups signed a letter led by the American Association of Persons with Disabilities, "strongly urging policymakers to reject potentially catastrophic legislation and policies that reference QALYs and similar metrics."[90] Even leading academics who have long relied upon QALYs for their work, have acknowledged that "the problem of whether [QALYs] unjustly discriminate[s] against the disabled remains a deep and unresolved difficulty."[91]

PhRMA also strongly recommends that CMS commit to avoiding reliance on CEAs, regardless of the metric it is rooted in, when determining a selected drug's MFP as part of this process. Reliance on CEA, whether it is rooted in QALYs or another similar metric, as the basis for policy decisions risks further discriminating against underserved and underrepresented people of color who are already at higher risk of not receiving the care they need. Given CMS' priority to improve health equity, this should be of particular concern. According to Tufts Medical Center, fewer than five percent of CEAs stratify results by race or ethnicity.[92] And because CEA ignores important patient differences in communities of color – such as differences in treatment, disease risk, health status, or life expectancy – it ignores (and potentially worsens) systemic inequities that harm people in those communities. For example, as Black seniors are more likely to die of colon cancer,[93] some treatments have been

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[88] SSA § 1182(e).
[89] National Council on Disability. (2021). NCD Letter to Congress recommending QALY ban in Build Back Better Act. Available at: https://ncd.gov/publications/2021/ncd-letter-qaly-ban.
[90] American Association of People with Disabilities. (2021). "Reject Health Policies that Discriminate." Available at: https://www.aapd.com/wp-content/uploads/2021/04/Reject-Health-Policies-that-Discriminate-1.pdf.
[91] Neumann P, Sanders G, et al. (2017). Cost Effectiveness in Health and Medicine, Second Edition.
[92] Lavelle TA, Kent DM, Lundquist CM, Thorat T, Cohen JT, Wong JB, Olchanski N, Neumann PJ. (2018). Patient Variability Seldom Assessed in Cost-effectiveness Studies. Med Decis Making. 38(4):487-494. DOI: 10.1177/0272989X17746989. Epub 2018 Jan 19. PMID: 29351053; PMCID: PMC6882686.
[93] Office of Minority Health. (2021). "Cancer and African Americans." Available at: https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=16.

estimated to be more effective in improving survival among Black patients relative to other races.[94] CEA, which determines what works for an average patient population, would obfuscate the value of treatments to Black patients.

QALY-based CEA also often assigns a lower value to Black lives. Researchers found that the life of a Black patient with diabetes and visual impairment is valued as having 15 percent fewer QALYs remaining compared to White patients with the same diseases.[95] Additionally, QALY-based research systematically undervalues communities of color because they have lower life expectancy relative to the average population[96] due to factors including worse access to care,[97] lower quality of care,[98] and higher risk of disease.[99] As a result of shorter life expectancies, Black patients' lives would be automatically valued ten percent less than White patients.[100]

CEA based on any metric can present significant concerns beyond those issues related to discrimination, as it often fails to capture benefits and impacts that matter to patients or patient subgroups. For example, generic measures, such as the EQ-5D, are often used for capturing patients' health-related quality of life to assess QALYs.[101] While these types of measures are useful for simplifying the comparison of different interventions, they do not always capture all the dimensions of quality of life that are important to patients. For example, researchers have noted that the EQ-5D may fail to reflect the entirety of quality of life for patients with sickle cell disease by not including domains such as fatigue, stigma, fluctuations in pain (particularly from recurrent painful vaso-occulusive events or pain crises), or the impact of racial disparities all of which are relevant for people with sickle cell disease.[102,103]

We caution against use of metrics that seek to address the discriminatory nature of QALYs, but have their own flaws. In addition to documented equity and technical issues, these measures have been shown to inaccurately and incompletely capture the full impact of treatments on patients. For example, in response to the controversy surrounding QALYs, the Institute for Clinical and Economic Review (ICER) developed a new metric for quantifying value, the equal-value life year gained (evLYG).[104] However, the evLYG introduces new problems. For example, the evLYG devalues drugs for conditions that do not extend life expectancy, like eczema or blindness, so therapies for these conditions would be seen as having no value.[105] Thus, the evLYG would value

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[94] Mack CD, Carpenter W, Meyer A, Sanoff H, Stürmer T . (2012). "Racial Disparities in Receipt and Comparative Effectiveness of Oxaliplatin for Stage III Colon Cancer in Older Adults." Available at: https://acsjournals.onlinelibrary.wiley.com/doi/pdfdirect/10.1002/cncr.26622.

[95] McCollister K, Zheng DD, Fernandez CA, Lee DJ, Lam BL, Arheart KL, Galor A, Ocasio M, Muennig P. (2012). "Racial Disparities in Quality-Adjusted Life-Years Associated with Diabetes and Visual Impairment. Diabetes Care. 35; 1692-1694. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3402250/pdf/1692.pdf.

[96] Arias E, Tejada-Vera B, Ahmad F, Kochanek KD. (2021). "Provisional Life Expectancy Estimates for 2020." Vital Statistics Rapid Release. Available at: https://www.cdc.gov/nchs/data/vsrr/vsrr015-508.pdf.

[97] Centers for Disease Control and Prevention. (2021). "Health Equity Considerations and Racial and Ethnic Minority Groups." Available at: https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html.

[98] Broder M., Ortendahl J. (2021). "Is Cost-Effectiveness Analysis Racist?" PHAR. Available at: https://blogsite.healtheconomics.com/2021/08/is-cost-effectiveness-analysis-racist/.

[99] Office of Minority Health. (2018). "Minority Population Profiles." Available at: https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=2&lvlid=26.

[100] Broder M., Ortendahl J. (2021). "Is Cost-Effectiveness Analysis Racist?" PHAR. Available at: https://blogsite.healtheconomics.com/2021/08/is-cost-effectiveness-analysis-racist/.

[101] Mott, D., Kumar, G., Sampson, C., Garau, M. (2021) How is Quality of Life Measured for Health Technology Assessments? Office of Health Economics. Available at: https://www.ohe.org/publications/how-quality-life-measured-health-technology-assessments.

[102] Mott, D., Garau, M. (2022). When Generic Measures Fail to Reflect What Matters to Patients: Three Case Studies. Office of Health Economics. Available at: https://www.ohe.org/publications/when-generic-measures-fail-reflect-what-matters-patients-three-case-studies#.

[103] Power-Hays, A., McGann, P. T. (2020). When Actions Speak Louder than Words – Racism and Sickle Cell Disease. N Engl J Med; 383:1902-1903.DOI: 10.1056/NEJMp2022125.

[104]ICER. (2018). "The QALY: Rewarding the Care that Most Improves Patients' Lives. Available at: https://icer.org/wp-content/uploads/2020/12/QALY_evLYG_FINAL.pdf.

[105] Cohen JT, Ollendorf, DA, Neumann PJ. (2018). "Will ICER's Response to Attacks on the QALY Quiet the Critics?" Tufts Center for the Evaluation of Value and Risk in Health. Available at: https://cevr.tuftsmedicalcenter.org/news/2018/will-icers-response-to-attacks-on-the-qaly-quiet-the-critics.

two drugs, one that reduces side effects and one that does not, as of equal value, even though side effects have a significant impact to patients. Neither the QALY nor the evLYG properly captures the value of a drug to patients and people with disabilities, and CMS should avoid reliance on either.

Furthermore, PhRMA has significant concerns about how CMS intends to implement the statutory prohibition on use of QALYs and similar metrics, critical to protecting patients and persons with disabilities, many of whom strongly oppose these standards. In the Guidance, CMS states that in situations where a study uses QALYs but also has "clearly separated" this use from other evidence in the study that is relevant to the price-setting factors, CMS will consider this "separate evidence." CMS also notes that it will "ask" entities to state whether or not the research submitted contains QALYs, thus placing the responsibility entirely on CMS to ensure that QALY-based research is not considered in determining MFPs for selected drug. Beyond those statements there is a worrisome lack of specifics offered as to how CMS intends to operationalize and enforce the QALY prohibition. When combined with the overall lack of transparency in CMS' decision making, this proposal is likely to erode public trust in the program.

As it stands, CMS does not have the time and expertise to review large quantities of data and separate out the information in the study that is relevant to the price-setting factors but does not implicate the use of QALYs. Further, CMS fails to define "clearly separated" sufficiently to allow stakeholders to understand what information is prohibited and what is not. It is unclear to what degree any influence QALY-based research has on other parts of research that are not QALY-based automatically disqualifies the non-QALY based research from consideration. Instead of allowing CMS to judge the separation, CMS should require that entities submitting information have removed QALY-based information. Often, non-QALY driven comparative effectiveness research is not easily cleaved from its QALY-based parts. ***PhRMA recommends that CMS require that any entity submitting information attest to having removed QALY (or similar metric)-based research from its submission.***

h. Standards for Review of Literature and Research (Section 50.2)

In describing the approach it will take to determining MFPs for selected drugs, CMS states that it intends to review existing literature and real-world evidence (RWE). In a single sentence, CMS also describes criteria it may consider in determining the literature it intends to review as part of setting MFPs. While PhRMA appreciates CMS offering these criteria, we believe that this falls far short of what is necessary to ensure that the evidence CMS relies upon is fit for purpose. For example, CMS states that it will consider "rigor of the study methodology" but does not describe what qualifies as methodologically rigorous or cite examples of third-party standards that evidence must meet to be considered.

Failure to provide clarity around the quality and characteristics of evidence CMS intends to consider will undoubtedly undermine CMS' methodology for setting prices in the eyes of manufacturers and other stakeholders, and deprive manufacturers of necessary predictability in terms of how CMS will arrive at MFPs. Therefore, ***PhRMA recommends that CMS go several steps further, and develop robust standards it will adhere to ensure that the evidence it both relies upon and develops is methodologically rigorous and patient-centered.*** The development of such standards is critical to giving manufacturers, as well as other stakeholders, confidence in the research CMS develops and relies upon in determining MFPs.

Standards for quality and patient-centeredness are not only critical for third-party evidence reviewed by CMS, but for CMS' internal analysis as well. CMS notes in section 50.2 that in addition to reviewing existing literature, it will also "conduct internal analytics", though it does not provide further detail on what those analytics might entail. It also does not appear from the Guidance that CMS intends to apply the aforementioned criteria to its own analysis, which is concerning. It is not only critical that external evidence CMS considers be methodologically rigorous and patient-centered, but that CMS' own analyses achieve these goals. Therefore, ***PhRMA recommends that CMS clarify that its own internal analytics will be required to meet well-defined quality standards as well.***

There is a significant body of work that CMS may choose to borrow from in developing standards for rigor and patient-centeredness. Several organizations have done work to create best practices, guiding principles and guidelines in establishing principles and standards for evidence and data. CMS should pay particular attention to the standards set forth by patient advocacy organizations such as the National Health Council, which have also developed their own guidance in evaluating the quality and patient-centeredness of value assessment frameworks.[106] The National Health Council has developed a rubric for Patient Centered Value Assessment,[107] which outlines six key domains[108] that PhRMA agrees are critical to ensuring the evidence and organizations CMS relies upon in determining a selected drug's MFP are of high-quality and are patient-centered. The rubric also contains additional details on specific domains that CMS should reference when developing its own standards.

CMS should look to academically driven organizations as well. For example, the International Society for Pharmacoepidemiology (ISPE) created "Guidelines for Good Pharmacoepidemiology Practices (GPP)," which propose essential practices and procedures that should be considered to help ensure the quality and integrity of pharmacoepidemiologic research, and to provide adequate documentation of research methods and results.[109] While adherence to these guidelines does not ensure valid or robust research, they provide a starting point in achieving a methodologically sound framework for the research and data CMS plans to both conduct and review as part of MFP setting.

PhRMA has public, well-established principles[110] on evidence-based medicine and value assessment that reflect the consensus and knowledge of experts in the biopharmaceutical industry. While these best practices focus on value assessment in the context of private sector decision-making, there is still significant relevance in their content. The National Pharmaceutical Council also has detailed guiding practices for value assessment.[111]

Academics and researchers such as the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Special Task Force on U.S. Value Assessment Frameworks have established best practices for health technology assessments (HTA). While the Task Force recommendations extend beyond the scope of review established in the IRA (e.g., by making recommendations related to cost-effectiveness analysis), they do illustrate the importance of CMS considering a broad range of value elements (e.g., fear of contagion, scientific spillover).

i. Standards for Third Parties Conducting Technology Assessments (Section 50.2)

CMS also notes that it will "consult subject matter experts as part of its process to set MFPs for selected drugs, in addition to considering evidence from "the Primary Manufacturer and members of the public, including other manufacturers, Medicare beneficiaries, academic experts, clinicians, and other interested parties." However, CMS has thus far failed to provide any information to the public about what third-party evidence it will rely upon in making MFP determinations. Building on our recommendation above that CMS create robust standards for the evidence it will consider in determining MFPs (as discussed above), ***PhRMA recommends CMS set standards in***

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[106] National Health Council. (2021). Value Classroom. Available at: https://nationalhealthcouncil.org/education/value-classroom/.
[107] National Health Council. (2016). The Patient Voice in Value: The National Health Council Patient-Centered Value Model Rubric. Available at: https://nationalhealthcouncil.org/wp-content/uploads/2020/11/20160328-NHC-Value-Model-Rubric-final.pdf.
[108] These domains include: (1) Patient Partnership, (2) Transparency to Patients, (3) Inclusiveness of Patients, (4) Diversity of Patients/Populations, (5) Outcomes Patients Care About, (6) Patient-Centered Data Sources. Learn more at: https://nationalhealthcouncil.org/wp-content/uploads/2020/03/NHC-One-Pagers_Domains.pdf.
[109] Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making, available at: https://www.ispor.org/docs/default-source/publications/newsletter/rwe-data-treatment-comparative-effectiveness-guideline.pdf.
[110] PhRMA. (2016). Principles for Value Assessment Frameworks. Available at: https://phrma.org/resource-center/Topics/Cost-and-Value/Principles-for-Value-Assessment-Frameworks.
[111] National Pharmaceutical Council. (2016). Guiding Practices for Patient-Centered Value Assessment. Available at: https://www.npcnow.org/guidingpractices.

guidance that external organizations for organizations conducting evidence synthesis or technology assessment must meet.

Such standards should ensure methodological rigor and necessarily exclude organizations with a payor-focused mission or funding, as well as organizations that historically focus on CEA. This is important because of statutory prohibitions against CEA as well as the need to avoid analysis driven by a payor focus on cutting costs over patient needs by discounting clinical and non-clinical benefits that matter to patients, caregivers and society.

Adherence to appropriate standards for patient-centeredness and methodological rigor will result in avoidance of certain organizations that fail to meet those standards. In this regard, PhRMA urges CMS not to rely on evidence generated by the ICER or similar cost effectiveness analysis-driven organizations. ICER's grounding in threshold-based decision making, payor-centered mission, and methodological shortcomings make it and similar organizations ill-suited to the standards set in the IRA, as well as the goals of patient-centeredness and public trust. While many stakeholders have voiced particular concern over ICER's methods and governance, CMS should generally avoid relying on any technology assessment organizations that cannot demonstrate clear independence and patient-centeredness. This should also preclude reliance on other technology assessment organizations that primarily serve or are governed by payors, such as the Blue Cross Blue Shield Technology Evaluation Center or the Drug Effectiveness Review Project.

To date, ICER has fallen short of the types of standards that CMS should develop for setting the MFP. ICER's bias toward payor needs and cost-cutting has been seen in its drug-specific assessments, which often deviate from its own commitments to stakeholders to obtain predetermined, payor-driven objectives. Several months before ICER's assessment of remdesivir, a treatment for COVID-19, ICER committed to include the societal perspective as a co-base case alongside the health system perspective in its assessments, when disease areas met certain criteria.[112] However, in spite of its prior commitment – and COVID-19 clearly meeting the established criteria – ICER declined to develop a co-base case based on the societal perspective, resulting in a skewed assessment of remdesivir's value. This ignored important societal benefits of an effective treatment for COVID-19, such as reducing the risk associated with reopening business and schools. ICER was criticized for this decision, not only by the biopharmaceutical industry, but by former employees and academic thought-leaders.[113]

ICER's assessments have also fallen short of standards for patient-centeredness in evidence assessment. Although ICER includes outcomes that matter to patients and caregivers in the "other benefits and disadvantages" or "contextual consideration" portion of its report, it fails to include the outcomes in its recommendations on its health-benefit price benchmark of a drug. For example, in ICER's review of treatments for myasthenia gravis, ICER omitted multiple outcomes from its quantitative assessment of the treatment's value, including impact on caregivers, chronic fatigue, and impact on mental health, that were cited by patient and caregiver advocates as important.[114]

Importantly, ICER's assessments heavily rely on the QALY metric, which as discussed above has a history of devaluing the lives of vulnerable populations. While it is now recognized by many stakeholders and researchers that traditional methods of QALY-based value assessment are controversial and outmoded (and ICER itself has acknowledged these concerns[115]), ICER persists in generating health-benefit price benchmarks based on QALYs and similarly flawed metrics for every assessment it conducts. ICER's failure to acknowledge the concerns of

[112] Institute for Clinical and Economic Review. (2020). 2020 – 2023 Value Assessment Framework. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_2020_2023_VAF_102220.pdf.
[113] Cohen, J. T., Neumann, P. J., Ollendorf, D. A. (2020). Valuing And Pricing Remdesivir: Should Drug Makers Get Paid For Helping Us Get Back To Work? Health Affairs Forefront. Available at: https://www.healthaffairs.org/do/10.1377/forefront.20200518.966027/full/.
[114] ICER. (2021). Eculizumab and Efgartigimod for the Treatment of Myasthenia Gravis: Effectiveness and Value. Available at: https://icer.org/wp-content/uploads/2021/03/ICER_Myasthenia-Gravis_Final-Report_12-Month-Check-Up_12122.pdf.
[115] ICER. (2018). The QALY: Rewarding the Care That Most Improves Patients' Lives. Available at: https://icer-review.org/wp-content/uploads/2018/12/QALY_evLYG_FINAL.pdf.

stakeholders with regard to the QALY and other issues is why CMS should avoid reliance on ICER and other similar organizations when determining MFPs.

j. Consideration of Real-World Evidence (Section 50.2)

We appreciate CMS' statement that it will consider RWE as part of its process for setting MFPs. PhRMA hopes that in determining MFPs for selected drugs, CMS will review and incorporate a broad range of rigorous scientific evidence, including data resulting from real-world experience with the drug's use, including the RWE that has become available in the years since a treatment's FDA approval.

However, we are concerned by 1) the lack of specifics in the Guidance as to the standards for quality CMS will use to determine whether individual pieces of RWE should be relied upon to determine MFPs, and 2) the lack of specifics as to how RWE will be weighed against other forms of evidence. These are important details that manufacturers, as well as other stakeholders, require in order to understand how CMS intends to arrive at MFPs for selected drugs.

RWE can come from a variety of sources, including electronic health records, payor administrative claims, implementation studies and patient registries and represents a valuable source of information about the real-world benefits and risks of a medicine. CMS should consider evidence from all these sources, and incorporate a broad range of rigorous scientific evidence, including data resulting from real-world experience with the drug's use, including the RWE that has become available in the years since a treatment's FDA approval.

Particularly for a drug that has been on the market seven or more years, RWE can provide valuable insights into how the drug works in a real-world clinical setting, including for different subpopulations and in different contexts. For example, an ongoing study of 133 people with HIV demonstrated the benefits of a long-acting antiretroviral treatment (LA-ART) to individuals with HIV. The study showed that the LA-ART given every four to eight weeks, and delivered with comprehensive support services, suppressed HIV in people who were previously not virologically suppressed. The study focused on reaching people who have historically had decreased access to antiretroviral therapy (ART), including people experiencing housing insecurity, mental illnesses, and substance use disorders, and who may have been included in clinical trials.[116]

However, use of RWE and the consideration and weight it is given varies amongst organizations and decision-makers. This makes it important for CMS to include more explicit discussion of its approach to considering RWE as part of its MFP methodology than what was included in the Guidance. ***PhRMA recommends that CMS appropriately consider rigorous RWE generated after initial FDA approval related to the benefits and impact of a selected drug.*** Consideration of RWE will be particularly important to ensure CMS can properly assess and value the full range of benefits and elements of unmet need discussed below, such as improved adherence, patient convenience, and broad health care cost offsets.

k. Consideration of Specific Patient Populations (Section 50.2)

CMS states that it will consider research on and RWE relating to Medicare populations – including individuals with disabilities, end-stage renal disease (ESRD) and aged populations – as particularly important. In addition, CMS will prioritize research specifically focused on these populations over studies that include outcomes for these populations, but in which these populations were not the primary focus. CMS states that it will consider the effects of the selected drug and its therapeutic alternative(s) on specific populations, including individuals with disabilities, the elderly, the terminally ill, and children.

[116] Long-acting antiretroviral therapy suppresses HIV among people with unstable housing, mental illnesses, substance use disorders. (Feb 21, 2023). Available at: https://www.nih.gov/news-events/news-releases/long-acting-antiretroviral-therapy-suppresses-hiv-among-people-unstable-housing-mental-illnesses-substance-use-disorders.

Because patient sub-populations can differ in their response to or preference for a therapy, a variety of treatment options may be required to optimize treatment and provide the most clinical benefit to a patient. CMS recognition of patient heterogeneity is particularly important to ensure alignment with the emergence of personalized medicine. While the sub-populations listed above are important, PhRMA recommends CMS consider additional subgroups as well, including those based on factors such as genomics, preferences, co-morbidities, and marginalized populations experiencing avoidable disparities in health outcomes.

This consideration is critical because the value individual patients and patient subgroups place on benefits and impacts, or their unmet needs, can vary. Studies have long shown that not only do patients place significant emphasis on benefits other than prolonged survival or cost, but that these preferences vary considerably depending on factors such as type and severity of disease and individual life circumstances. For example, research has shown that when asked to weigh different treatment impacts (e.g., effect on disease progression, effect on relapse rate, effect on multiple sclerosis (MS) symptoms), preferences among patients with MS were highly diverse. In most categories, patient opinions were more varied than those of other stakeholders, including clinicians or payors.[117] In order to capture this diversity, CMS needs to consider all relevant sub-populations for the selected drug.

III. Negotiation Process (Section 60)

Section 1194 of the SSA, requires a "consistent methodology and process" for setting MFPs, and that these prices be "fair." CMS has a critical opportunity to design this consistent methodology to ensure fair prices that account for reduced access to medicines in Medicare and loss of future treatments and cures.

Unfortunately, CMS' Guidance provides no assurance that the Agency will meet this standard. Rather than describing a "consistent methodology and process," CMS proposes an unworkable and subjective framework for setting MFPs. Furthermore, the process for price setting signals that CMS intends to provide only the most limited opportunities for stakeholders, such as patients and clinicians, to have input into the Program.

While CMS recognizes the importance of ensuring the rigor of the research and evidence synthesis it relies on in MFP decision-making, the Guidance fails to describe a process or standards for ensuring that its MFP determinations are rooted in patient-centeredness and methodological rigor. To help address this, ***PhRMA strongly recommends that prior to making its initial offer to the manufacturer, CMS make available to the public key elements of its MFP analysis. and provide an opportunity for the public to comment on them. This should include, but not be limited to:***

- ***Therapeutic alternative(s) CMS has identified for any selected drug it is considering (for each indication);***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS;***
- ***Benefits and impacts of a selected drug CMS intends to consider; and***
- ***Stakeholders, and other government agencies and organizations CMS intends to engage, formally or informally.***

Below we outline specific concerns with the proposals in the Guidance, as well as concrete recommendations for how CMS can address these concerns, mitigate harm to patients, and recognize innovation in implementing the Program.

[117] Nash, B. Mowry, S. McQueen, R. B., Longman, R. (2017). People with MS value therapies differently than do physicians or payers. Available at: https://realendpoints.com/wp-content/uploads/2017/12/PhRMA-white-paper-final.pdf.

a. Price Setting Methodology

CMS proposes as potential starting points for the initial offer: 1) Part D net price or Part B average sales price (ASP) of the selected drug; 2) Part D net price(s) and/or Part B ASP of therapeutic alternative(s); or 3) FSS or "Big Four" Agencies price either for selected drugs with no therapeutic alternative(s) or for selected drugs that have therapeutic alternative(s) with net prices or ASPs greater than the statutory ceiling. This approach is misguided and will result in egregiously low prices previously criticized and rejected by stakeholders. Furthermore, the approach proposed by CMS is arguably in tension with the statute. While the statute requires CMS to achieve the lowest "fair" price "for each selected drug,"[118] CMS' approach looks primarily at therapeutic alternative(s) to the selected drug, rather than the selected drug itself.

The approach relies upon therapeutic reference pricing, which resembles the "least costly alternative (LCA)" policies previously attempted by CMS and struck down by a federal court more than a decade ago.[119] This approach would give CMS broad authority to make judgments about clinical "similarity" for a broad range of medicines. It would also overlook significant differences in the needs of patients, many of whom do not fit value judgments based on broad, average results. Individual patient differences occur due to several factors, such as genetic variation, differences in clinical characteristics, co-morbidities, and quality-of-life preferences. For example, the five different larifuno-oncology agents recommended for treatment of metastatic non-small cell lung cancer (mNSCLC) can appear similar when looking at treatment effects based on averages,[120] however, different treatments are recommended based on patient subgroup[121] – defined by PD-L1 expression – because overall survival can increase by as much as 164 percent[122] based on the patient characteristics. Furthermore, patients can value quality-of-life factors differently with treatments that require less frequent visits to a provider or that can be delivered by mail often being of higher value to Hispanic and Black patients who are more likely to live in a neighborhood impacted by pharmacy deserts. As a result, imposing policies like LCA that rely on broad judgments of comparative effectiveness of treatments will overlook important differences in the way individual patients respond to treatment, and downstream, can create barriers to access to important treatments. When proposed in other contexts, patient advocates have reiterated these concerns, "We cannot achieve a healthier society simply by making investments based on what is the cheapest."[123]

Furthermore, PhRMA does not support CMS' proposed reliance on the FSS price or the "Big Four" price. Domestic reference pricing at these prices has also been soundly rejected by policymakers, including very recently by Congress – during Senate floor consideration of the IRA, Senator Bernie Sanders offered an amendment to tie drug prices in Medicare to those used in the VA. This amendment failed overwhelmingly by a vote of 99 to one.[124]

FSS contracts are not designed or intended to establish a pricing benchmark for medicines, and instead are procurement contracts that direct federal purchasers use to purchase items and services from vendors and suppliers. Specifically, FSS purchasers acquire medicines on the FSS directly from wholesalers or biopharmaceutical manufacturers at the contracted price and then furnish such medicines to certain patients within "closed" health care delivery systems. Further, FSS and "Big Four" prices do not reflect the full "cost" of the

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[118] 42 U.S.C. § 1320f-3(b)(1).
[119] Available at https://ecf.dcd.uscourts.gov/cgi-bin/show_public_doc?2008cv1032-22.
[120] Cui P, Li R, Huang Z, Wu Z, Tao H, Zhang S, Hu Y. (2020). "Comparative effectiveness of pembrolizumab vs nivolumab in patients with recurrent or advanced NSCLC." Nature. 10:13160. Available at: https://doi.org/10.1038/s41598-020-70207-7.
[121] Bradley CA. (2019). "Pembrolizumab improves OS across PD-L1 subgroups." Nature Reviews. 16; 403. Available at: https://www.nature.com/articles/s41571-019-0213-5.pdf?origin=ppub.
[122] Mok TS, Wu Y, Jydaba I, Kowalski DM, Cho BC, Turna HZ, et al. (2019). "Pembrolizumab versus chemotherapy for previously untreated, PD-L1-expressing, locally advanced or metastatic non-small-cell lung cancer (KEYNOTE-042): a randomised, open-label, controlled, phase 3 trial." The Lancet. 393: 10183; 1819- 1830. Available at: https://doi.org/10.1016/S0140-6736(18)32409-7.
[123] Thorpe, K. (2014). MedPAC recommendations miss the mark. The Hill. Available at: https://thehill.com/blogs/congress-blog/healthcare/203976-medpac-recommendations-miss-the-mark/.
[124] S. Amdt. 5210 to S. Amdt. 5194 to H.R 5376 https://www.senate.gov/legislative/LIS/roll_call_votes/vote1172/vote_117_2_00288.htm.

medicine. As noted in a recent report by the CBO, comparing prescription drug prices among government programs is difficult, and average prices are not directly comparable because the price of medicines in federal programs like Medicare, which uses a retail distribution network, must consider pharmacy storage and dispensing costs and profits. In contrast, average FSS and "Big Four" prices (which are two distinct prices authorized by law for different purchasers) do not consider wholesaler profits, storage, distribution, or pharmacy/physician dispensing.[125] They are, therefore, not reasonable starting points for CMS' price setting process.

In addition, reliance on FSS and "Big Four" prices could result in manufacturers effectively being assessed an inflation rebate twice. Per statutory requirements of the Veterans Health Care Act, some medicines on the FSS have an additional inflationary rebate component factored into the Federal Ceiling Price, while medicines in Medicare will have a separate inflation rebate if pricing metrics increase faster than inflation.[126]

Recommended Approaches to Determining MFPs for Selected Drugs

PhRMA believes that instead of haphazardly piecing together an approach to price setting based on previously rejected policy ideas, CMS should adopt a methodology in the initial years of the program that acknowledges both the exceptionally challenging task at hand, as well as the substantial potential harm to patients and innovation if CMS undervalues selected medicines. It is broadly understood that CMS is establishing a price setting program for the first time, without necessary experience in this area. There is also extraordinary burden on manufacturers to submit data and engage in this complicated process with little information or advance notice. Given this confluence of factors, ***PhRMA recommends that CMS ensure all MFPs are set at the statutory ceiling price beginning with IPAY 2026, and for several subsequent price applicability years.***

Beyond the first several years of the Program, CMS should consider the fundamental problems posed by the IRA's price setting framework and work to adopt policies that mitigate those problems. One example is the reduced incentives for continued R&D for small molecule medicines created by the IRA's criteria for selecting drugs, which could result in CMS selecting small molecule drugs a mere seven years after their initial FDA approval. The IRA effectively reduces the period of exclusivity from the current effective average of 13 to 14 years to nine years for small molecule drugs selected for price setting (and CMS' decision to finalize a "qualifying single source drug" (QSSD) definition based on active moiety heightens this effect).[127] Nine years will simply not be enough time for many drugs in development to earn a return that warrants the large and uncertain investment a company must make to bring a drug to market. Recent empirical research shows that, on average, about half of a product's revenues are earned during years 10 through 13 after approval, and very few drugs have earned a return justifying investment within nine years after approval.[128] And as previously noted, recoupment of investment itself isn't sufficient –-a "cost-plus" approach to setting MFPs will also undoubtedly devastate biopharmaceutical innovation.

For these reasons, ***PhRMA recommends setting the MFP for selected drugs that have been on the market for less than 13 years at or near the ceiling price set forth in statute.*** This would be in keeping with the overall intent of the IRA, which sets ceiling prices at different levels according to the time since FDA approval.

CMS should also recognize in setting MFPs that the stated intent of the price setting provisions was to address the lack of competition for older drugs from generics or biosimilars. This objective takes a narrow view of

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[125] CBO. (2021). A Comparison of Brand-Name Drug Prices Among Selected Federal Programs. Available at: https://www.cbo.gov/publication/57007. CBO notes that FSS and "Big Four" prices are not retail prices. Specifically, "Pharmacy dispensing fees are incorporated into the prices in Medicare Part D, Medicaid, and the TRICARE retail pharmacy network. However, the prices for VA and DoD…do not include the agencies' costs of dispensing drugs."

[126] See SSA §§ 1847A(i) and 1860D-14B.

[127] Grabowski H, Long G, Mortimer R, Bilginsoy M. (2021). Continuing trends in U.S. brand-name and generic drug competition. J Med Econ.;24(1):908-917. DOI: 10.1080/13696998.2021.1952795. PMID: 34253119.

[128] Tewari, A. et al. (2022) The Drug Pricing Handbook - Everything you Need to Know. Jefferies Research. September 15, 2022. p.4.

competition: for some products, brand-to-brand competition occurs prior to generic or biosimilar entry, which has resulted in payors negotiating steep rebates and a net price that falls below the statutorily mandated discount. CMS has an opportunity to acknowledge this competition by setting MFPs for such drugs at the ceiling price.

The statutory ceiling price for selected drugs is the lower of two options – either the net price (or ASP) of a selected drug, or a significant percentage off of the selected drug's non-FAMP. ***PhRMA recommends that if a selected drug's statutory ceiling price is the net price, then the MFP should be set at the ceiling price (the net price) for the selected drug.*** This would acknowledge drugs for which brand-to-brand competition has resulted in meaningful savings, and therefore, were not the target of the policy. Furthermore, it is operationally feasible for CMS, as CMS has access to the necessary price data and must calculate a net price to determine the ceiling price.

There are two other instances in which PhRMA specifically recommends CMS set the MFPs at the ceiling price beyond the first several years of the Program: drugs that represent a substantial unmet need and drugs that represent a significant therapeutic advance against therapeutic alternative(s). Identifying these types of discrete factors or circumstances that will result in MFPs at or close to the ceiling price would provide at least some predictability in CMS' decision-making process. Those recommendations are discussed below in subsections (f) (Unmet Medical Need) and (g) (Therapeutic Advance).

b. Weighting of Factors

As noted by CMS in the Guidance, the statute establishes two sets of factors that CMS must consider when determining the offers and counteroffers to reach a drug's MFP: "manufacturer-specific data" and evidence regarding alternative treatments. As CMS has acknowledged, the statute does not specify "how CMS should determine an initial offer nor how or to what degree each factor should be considered."[129] PhRMA is concerned by CMS' failure to clarify how it will use its discretion in considering and weighting the factors. ***PhRMA strongly recommends that CMS generally place greater emphasis on the factors related to the benefits medicines offer to patients included in section 1194(e)(2).*** These benefits include not just the benefit to patients, but also to caregivers and society. An emphasis on these benefits and factors may somewhat mitigate against the disincentives inherent in government price setting for continued innovation resulting from price setting by reducing the penalty on drugs with significant demonstrated benefits that accumulate over the course of a product's life cycle. We note, however, that the mitigation is limited by the fact that the statutory ceiling price applies even when a higher price would be set based on the factors related to the therapeutic benefits medicines offer to patients.

As a corollary, CMS should place less weight on factors that would diminish drugs' benefits and could stagnate innovation if overweighted. This includes most of the factors listed in section 1194(e)(1), such as cost of production, costs of R&D, and federal funding toward the development of a selected drug. If CMS places too much importance on these factors, the result could be a "cost recovery" pricing model for selected drugs, in which the price is set to allow the manufacturer to recoup only the cost of producing the drug, including the cost of R&D. Basing prices for drugs on costs incurred by the manufacturer, instead of the value and benefits conferred by the innovation, sends perverse, unintended signals to manufacturers that devalue and disincentivize R&D and pose a significant threat to innovation and progress for future medicines. Placing greater weight on the factors in section 1194(e)(2) will help incentivize continued medicine advances and innovation. In addition, to avoid a chilling effect on post-approval research, factors used to determine the MFP should include consideration of both existing and pending patent protections, existing regulatory data exclusivities, and labeled as well as pending indications in addition to other factors, such as ongoing clinical development programs.

[129] Guidance, section 60.3.

c. Therapeutic Alternative(s)

For IPAY 2026, CMS will identify the selected drug's FDA-approved indications that are neither excluded from coverage nor otherwise restricted. CMS will then identify pharmaceutical therapeutic alternative(s) for each indication of the selected drug, using data submitted by the Primary Manufacturer and the public, along with widely accepted clinical guidelines and peer-reviewed studies. CMS also will consider clinical evidence via literature searches.

Although PhRMA strongly disagrees with CMS' proposal to use therapeutic reference pricing as the starting point for MFP determinations, PhRMA agrees that therapeutic alternative(s) should generally be limited to pharmaceutical therapeutic alternative(s). We believe that some of the resources CMS cites in the Guidance, such as clinical guidelines, will be very helpful in identifying therapeutic alternative(s) for certain classes of drugs.

However, ***PhRMA believes that experts, including manufacturers and clinicians, should be the primary resources for determining therapeutic alternative(s), and CMS should go beyond what the Agency laid out in the Guidance to engage key stakeholders in the selection of therapeutic alternative(s).*** PhRMA notes that manufacturers are in a strong and unique position to inform CMS' determination of appropriate therapeutic alternative(s) for a selected drug, based on their extensive expertise and research on the benefits and impacts of their medicines throughout the product lifecycle. Manufacturer-sponsored research frequently includes comparative effectiveness research, which requires selection of a clinically appropriate comparator. Additionally, clinicians with disease-specific expertise and disease-specific clinical guidelines generated by clinicians should also play a meaningful role in CMS' determination of a selected drug's therapeutic alternative(s). Simply asking stakeholders to provide information through an ICR is an insufficient means of engaging stakeholders on this key issue. Clinician and patient engagement will be discussed in further detail in section III.t. of this letter.

Procedurally, it is unclear when CMS will identify the therapeutic alternative(s) for a selected drug and communicate that information to the manufacturer. PhRMA notes that if CMS fails to communicate the therapeutic alternative(s) for the selected drug early enough in the process, the manufacturer and stakeholders will be unable to include the required information in their data submissions to the Agency. ***PhRMA strongly recommends that CMS publicly identify the therapeutic alternative(s) selected, including if based on information and feedback received through the ICR, and allow the manufacturer and stakeholders to provide feedback on CMS' proposal.***

When determining the therapeutic alternative for a selected drug, ***PhRMA recommends that CMS use "clinical appropriateness" as the standard for decision-making.*** In order to determine the clinical appropriateness of a therapeutic alternative, CMS should do the following:

- Engage meaningfully with the manufacturer on potential therapeutic alternative(s) and comparator(s);
- Look to clinician guidance, including physician-driven evidence-based clinical guidelines, as a resource; and
- Reference other widely recognized, scientifically rigorous, evidence-driven resources to identify therapeutic alternative(s).

Selection of the appropriate therapeutic alternative(s) in assessments of the comparative effectiveness of treatments is complex and can involve subjective judgments. Both the significant complexity of this issue, as well as the consequences of CMS choosing an inappropriate therapeutic alternative for its decision-making, is illustrated in price setting systems outside the U.S. Germany provides perhaps the starkest case study for the magnitude of the impact that inappropriate comparator selection can have in a large market. Problems with comparator selection, combined with rigidity in accepting indirect comparisons, is one of the main failings of the German system. In Germany, 70 percent of assessments by the German Federal Joint Committee (G-BA) are

negative for non-orphan innovative medicines, and most rejections (72 percent) are for not presenting data against the G-BA chosen comparator.[130] Yet, research shows that in 43 percent of cases, medical societies opposed the comparator selected by the G-BA.[131]

Beyond ensuring that the chosen therapeutic alternative is clinically appropriate, ***PhRMA strongly cautions that cost cannot play a role in determination of a selected drug's therapeutic alternative or clinical comparator.***[132] Experience in other countries illustrates how cost factors have the potential to skew choice of comparators to achieve a desired cost-containment outcome. The Agency should establish standards and procedures for comparator selection that protect against this. In Germany, for example, because the price of a drug is based on its comparative clinical effectiveness relative to a comparator, Germany's choice for a comparator has a considerable impact on the reimbursement price.[133] Germany uses the least costly available comparator as the price benchmark when the G-BA determines there is no benefit, even if the treatments have differences that are significant from a patient or caregiver perspective, such as reduced side effects or mode of administration.[134] PhRMA strongly cautions against adopting this approach.

d. Benefits and Impacts

In assessing comparative effectiveness between a selected drug and therapeutic alternative(s), CMS plans to identify outcomes to evaluate for each of the selected drug's indications and consider the safety profiles. When evaluating clinical benefits of the selected drug and its therapeutic alternative(s), CMS intends to consider health outcomes, intermediate outcomes, surrogate endpoints, patient-reported outcomes, and patient experience.

PhRMA is deeply concerned with CMS' description of the outcomes that it will consider in determining how a selected drug compares to a therapeutic alternative, particularly the narrow and vague description of the outcomes that CMS will consider, as well as its failure to center the decision-making on patients. In order to preserve patient access and biopharmaceutical innovation, ***PhRMA recommends that CMS consider the broad range of benefits and impacts of a selected drug, with particular focus on those that are important to patients, caregivers, and society.*** CMS' statement that it intends to consider health outcomes such as changes in symptoms or other factors that are of importance to a person and patient-reported outcomes is insufficient reassurance that patients will play a meaningful role in determining what benefits and impacts are prioritized as part of CMS' decision-making process. As noted by the Patient-Centered Outcomes Research Institute (PCORI) in its 2022 review of 200 publications from a range of different health organizations related to the discussion of value, "When it comes to defining patient-centered value, most stakeholders agree that it includes health and non-health outcomes and monetary and non-monetary impacts that are defined based on patient goals, expectations, and experiences."[135]

It is widely recognized that patients value a range of benefits of medicines beyond clinical endpoints evaluated in research.[136] For example, benefits that may be valued by patients, but typically are not captured in research, include the range of potential side effects, impact on patients' ability to carry out basic functions, and quality of

[130] AMNOG Monitor. Early benefit assessment: detailed analysis of all G-BA resolutions. Avalable at: https://www.amnog-monitor.com/.
[131] Bleß et al., (2016). Impact of scientific opinions in the benefit assessment of medicinal products. IGES Institute.
[132] While we recognize the statute mentions the "costs of…existing therapeutic alternatives," CMS should only use this in determining a selected drug's MFP, not in its initial determination of a drug's therapeutic alternative(s).
[133] Sieler, S. R., T., Brinkmann-Sass, C., Sear, R. (2015). AMNOG Revisited. McKinsey & Company. Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/amnog-revisited.
[134] Ivandik, V. (2014). Requirements for benefit assessment in Germany and England-overview and comparison." Health Economics Review. Available at: http://www.healtheconomicsreview.com/content/4/1/12.
[135] Havjou, O., Bradley C., D'Angelo, S., Giombi, K., Honeycutt, A. (2022). Landscape Review and Summary of Patient and Stakeholder Perspectives on Value in Health and Health Care. PCORI. Available at: https://www.pcori.org/sites/default/files/PCORI-Landscape-Review-Summary-Patient-Stakeholder-Perspectives-Value-Health-Health-Care-August-2022.pdf.
[136] Neumann, P. J., Garrison, L. P., Willke, R. J. (2022). The history and future of the "ISPOR value flower": Addressing limitations of conventional cost-effectiveness analysis. Value in Health, 25(4), 558–565. Available at: https://doi.org/10.1016/j.jval.2022.01.010.

life. Other non-clinical-related benefits also can be very important, such as the utility of reduced frequency of dosing through a long-acting formulation and reduced caregiver burden. CMS should ensure that its evaluations of therapeutic advances capture the value of and give significant weight to these benefits and impacts in selected drugs' MFPs to maintain incentives for manufacturers to continue meeting these needs.

In addition to capturing this full range of outcomes, CMS' methodology should ensure that when patient, caregiver, or clinician perspectives differ from those of payors, the former are prioritized. A survey focused on MS that included patients, neurologists who treat MS, and payors found significant variability in the value of different impacts among the different stakeholder groups. For example, MS patients placed the most value on treatment of mobility and upper limb function, whereas neurologists placed the least value on this combination of symptoms.[137] CMS must not evaluate therapeutic advances in a vacuum.

As noted above, ***PhRMA believes that benefits and impacts of a selected drug compared to its therapeutic alternative(s) must incorporate consideration of a drug's impact on society, including benefits to patient caregivers and their families.*** CMS does not mention society or caregivers at all in the discussion of outcomes in the Guidance even though approximately one out of every five Americans is a caregiver.[138] Failing to account for the benefits and impacts of a medicine to society could inappropriately reduce CMS' determination of a selected drug's MFP. For example, a recent study found that inclusion of caregiver impacts can have a significant effect on an assessment of an intervention's value.[139] Important disease-related societal impacts, such as a reduction in costs associated with incarceration rates (such as with treatments for alcohol use or mental illness), environmental impacts, and the cost of social services, should also be included in the MFP determination.

When a drug provides a significant benefit to society, CMS should consider increasing the MFP accordingly, including setting the price at or near the statutory ceiling. This should include any selected drug that is a vaccine, due to the unique circumstances of vaccines and substantial patient and public health benefits that they confer. Vaccines represent some of the most impactful advances in public health, helping to prevent the spread of many infectious diseases and, in many parts of the world, eliminating some of the most devastating conditions. There is no better case study for the importance of vaccines than the biopharmaceutical industry's response to the recent COVID-19 pandemic. The importance of vaccination goes beyond global pandemics, however – in the U.S. today, 16 diseases are now preventable as a result of childhood vaccines,[140] and routine immunization of U.S. children born between 1994 and 2018 has prevented more than 419 million illnesses.[141] The IRA itself recognizes the unique importance of vaccines, eliminating patient cost sharing for adult vaccines under Medicare Part D. CMS should recognize this in setting final MFPs as well by accounting for vaccines' remarkable benefits to public health.

PhRMA also has concerns about CMS' approach to identifying benefits and impacts; CMS should meaningfully engage with manufacturers and patients to identify the relevant benefits and impacts, rather than predominantly relying on literature reviews or ICRs. Specific recommendations for how CMS should engage with patients and physicians are discussed in section III.t. of this comment letter.

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[137] Nash, B., Mowry, S., McQueen, R. B. (2017). People with MS value therapies differently than do physicians or payers. RealEndpoints. Available at: https://realendpoints.com/wp-content/uploads/2017/12/PhRMA-white-paper-final.pdf.

[138] National Alliance for Caregiving and AARP. (2020). Caregiving in the U.S. 2020. NAC. Available at: https://www.caregiving.org/research/caregiving-in-the-us/.

[139] Lin PJ, D'Cruz B, Leech AA, Neumann PJ, Sanon Aigbogun M, Oberdhan D, Lavelle TA. (2019). Family and Caregiver Spillover Effects in Cost-Utility Analyses of Alzheimer's Disease Interventions. Pharmacoeconomics;37(4):597-608. DOI: 10.1007/s40273-019-00788-3. PMID: 30903567.

[140] Centers for Disease Control and Prevention (CDC). (2019), Diseases & the Vaccines that Prevent Them. CDC. Available at: https://www.cdc.gov/vaccines/parents/diseases/index.html.

[141] CDC. (2022). VFC Infographic: Protecting America's Children Every Day. Updated 2021 analysis using methods from "Benefits from Immunization during the Vaccines for Children Program Era – United States, 1994 – 2021. *MMWR*. 25 April 2014. Available at: https://www.cdc.gov/vaccines/programs/vfc/protecting-children.html.

PhRMA notes that accounting for a broad range of benefits and impacts aligns with input from experts in the fields of comparative effectiveness research and HTA.[142] Best practices for HTA include capturing a range of potential "value elements," including treatment adherence, fear of contagion, the value of hope, and scientific spillover effects.[143] Although they may be difficult to quantify, individuals and organizations, such as the Innovation and Value Initiative,[144] are developing methods to incorporate some of these value elements, such as insurance value and real option value into research. CMS can contribute to progress in this field by identifying these outcomes as important in its MFP-setting deliberations.

Input from clinicians, patients and caregivers with disease-specific experience will be particularly important in order to accurately identify the benefits and impacts of a treatment that matters to patients, caregivers, and society. As such, CMS will need to establish a process to engage with stakeholders, beyond soliciting feedback through an ICR. ***PhRMA recommends that following the ICR and prior to CMS' initial offer, CMS engage the manufacturer and other stakeholders in direct conversations, in which the Agency shares the benefits and impacts it identified as meaningful through the ICR, as well as its own research, and allows the manufacturer and stakeholders to provide feedback on the Agency's findings.***

Second, CMS should be transparent with both manufacturers and stakeholders as to the benefits and impacts that CMS considered, and how the benefits and impacts influenced the MFP. PhRMA recommends CMS provide this detail in both the justification for CMS' initial MFP offer (section 1194(b)(2)(B)), as well as the explanation for a drug's MFP (1195(a)(2)). Specifically, ***PhRMA recommends that CMS include in its explanation of a selected drug's MFP a table listing the following elements:***

- ***The benefits and impacts across all indications, clinical and non-clinical, that CMS considered in its determination of a selected drug's MFP;***
- ***CMS' process for determining benefits and impacts to include in its determination of the MFP, including a list of each stakeholder consulted;***
- ***Information about the relative weight given to each benefit and impact considered during the determination of the MFP;***
- ***Source(s) of evidence for each benefit and impact; and***
- ***How each benefit and impact influenced the final MFP.***

CMS' assessment of how a drug performs on these benefits and impacts (derived from stakeholder feedback) should form the foundation of how it arrives at a selected drug's MFP. Furthermore, this level of transparency – balanced with important data protections – is imperative so that manufacturers and stakeholders can have confidence in CMS' conclusions, and so that manufacturers can plan for evidence generation in anticipation of their drug's selection for the Program.

e. Cost of Selected Drug and Therapeutic Alternative(s)

As previously stated, PhRMA has significant concerns with CMS' proposal to use therapeutic reference pricing as the foundation of its approach to setting prices for selected drugs. However, we recognize that the statute includes as a factor "the extent to which such [MFP] drug represents a therapeutic advance as compared to

[142] Neumann, P. J., Willke, R. J., Garrison, L. P. (2018). A Health Economics Approach to US Value Assessment Frameworks—Summary and Recommendations of the ISPOR Special Task Force Report. Value in Health, 21(2), 119–123. Available at: https://doi.org/10.1016/j.jval.2017.12.012.
[143] Neumann PJ, Garrison LP, Willke RJ. (2022). The History and Future of the "ISPOR Value Flower": Addressing Limitations of Conventional Cost-Effectiveness Analysis. Value Health; 25(4):558-565. DOI: 10.1016/j.jval.2022.01.010. Epub 2022 Mar 9. PMID: 35279370.
[144] The Innovation and Value Initiative. https://thevalueinitiative.org/.

existing therapeutic alternatives and the costs of such existing therapeutic alternatives," to the extent such information is available.

Should such information be available, PhRMA recommends that CMS interpret such language broadly, to include a consideration of a range of direct and indirect costs (such as the costs to caregivers, transportation costs, lost work time[145]), and cost savings associated with appropriate use of a selected drug. Medicines not only improve and save lives, but also frequently help avoid other, often costly, health care services, such as emergency room visits, hospital stays, surgeries, and long-term care.[146] Health cost savings due to improved use of medicines are well-documented in public programs, including Medicare. For example, as a result of seniors and people with disabilities gaining Medicare Part D prescription drug coverage, Medicare saved $27 billion due to improved adherence to congestive heart failure medications from 2010 to 2016.[147] Other federal agencies recognize these savings; the CBO explicitly accounts for Medicare savings from policies that increase the use of medicines due to reduced spending on other Medicare services.[148] By recognizing these savings in determining a selected drug's MFP, CMS can provide an important signal to innovators that it recognizes the importance of medicines' ability to save money for the health care system.

Additionally, PhRMA recommends that any data CMS relies upon to understand the cost of a drug reflect true net cost after rebates to Medicare. Manufacturers often pay substantial rebates to Medicare Part D plan sponsors and pharmacy benefit managers, but these price concessions are not reflected in Part D negotiated prices. According to government data, rebates can reduce average net costs for Part D plan sponsors by 40 percent or more for commonly used classes of medicines.[149] Government data also show that manufacturer rebates lowered total gross Part D expenditures by 22 percent in 2020[150] and that total Part D rebates paid by manufacturers increased by more than 400 percent between 2010 and 2020.[151] These findings underscore the importance of CMS ensuring the data it uses to set the MFPs for selected drugs account for manufacturer rebates. PhRMA understands that CMS plans to identify the price[152] of each therapeutic alternative covered by Part D, net of all price concessions, when developing a starting point for its initial MFP offer.

CMS should also account for the significant discounts on medicines provided under the 340B Drug Pricing Program. Ignoring these statutory discounts could lead to CMS setting an MFP that negatively impacts incentives for innovation. While the IRA forbids a duplicate 340B and MFP discount on a selected drug, without needed data for verification, manufacturers could be forced to pay steep discounts under both programs in addition to any commercial rebates owed to Part D plans and PBMs. Overall, 340B purchases are 17 percent of outpatient

[145] As of 2018, more than one in six Medicare beneficiaries – or 10.1 million people – were employed according to: Feder, J. M., Radley, D. C. (2020). COVID-19's Impact on Older Workers: Employment, Income, and Medicare Spending. The Commonwealth Fund. Available at: https://www.commonwealthfund.org/sites/default/files/2020-10/Jacobson_COVID_impact_older_workers_ib_v3.pdf.
[146] PhRMA. (2022). 2022 Industry Profile Toolkit: Better Use of Medicines Can Improve Health Outcomes and Reduce the Use of Costly Medical Care. Available at: https://phrma.org/resource-center/Topics/Research-and-Development/IndustryProfile-2022/2022-Industry-Profile-Toolkit-Better-Use-of-Medicines-Can-Improve-Health-Outcomes-and-Reduce-the-Use-of-Costly-Medical-Care.
[147] CMS Press Release. (2017). Nearly 12 million people with Medicare have saved over $26 billion on prescription drugs since 2010. Available at: https://www.cms.gov/newsroom/press-releases/nearly-12-million-people-medicare-have-saved-over-26-billion-prescription-drugs-2010.
[148] CBO.(November 2012). Offsetting Effects of Prescription Drug Use on Medicare's Spending for Medical Services. Available at: https://www.cbo.gov/sites/default/files/cbofiles/attachments/43741-MedicalOffsets-11-29-12.pdf.
[149] Medicare Payment Advisory Commission. (July 2022) A Data Book: Health Care Spending and the Medicare Program. Available at: https://www.medpac.gov/wp-content/uploads/2022/07/July2022_MedPAC_DataBook_SEC_v2.pdf.
[150] Ibid.
[151] Medicare Payment Advisory Commission. (2022). Initial findings from MedPAC's analysis of Part D data on drug rebates and discounts. Available at: https://www.medpac.gov/wp-content/uploads/2021/10/MedPAC-DIR-data-slides-April-2022.pdf.
[152] However, release of these data has significant competitive implications well beyond the Medicare program. Thus, specific pricing information by competitive products should never be shared.

branded drug sales.[153] Thus, if CMS were to ignore 340B discounts it would be missing a key factor that economists have stated can impact drug pricing.[154]

f. Unmet Medical Need

PhRMA has significant concerns with CMS' unnecessarily narrow definition of "unmet medical need." CMS states that it will consider a selected drug as filling an unmet medical need if it treats a disease or condition where there are very limited or no other treatment options. In defining unmet medical need narrowly, CMS will exacerbate the harm to innovation that will result from Medicare price setting. If CMS fails to fully acknowledge innovation that addresses unmet patient needs, it will send signals that disincentivize ongoing innovation in areas where patients desperately need options.

CMS' definition is far narrower than the definition relied upon by the FDA, which facilitates several expedited programs (e.g., accelerated approval, breakthrough designation). In order to determine if a product meets the threshold for these programs, FDA defines unmet medical need as "a condition whose treatment or diagnosis is not addressed adequately by available therapy" that includes either "an immediate need for a defined population" or "a longer-term need for society."[155] FDA further clarifies that such a drug will treat a condition:

- Where there is no available therapy;
- Where there is available therapy, but the drug presents additional benefits; and
- Where the only available therapy was approved under the accelerated approval program and clinical benefit against the primary endpoint has not yet been verified.

Research has shown that the FDA definition of unmet need has significantly benefited patients by allowing the FDA to prioritize drugs that offer the largest health gains.[156] Therefore, given the significant risks to patients from CMS' inexplicably narrow definition, ***PhRMA recommends that at a minimum, CMS set the MFP for any selected drug that meets the FDA's definition of unmet need at the ceiling price, including those that met that definition at the time of approval.***

Furthermore, CMS should recognize other types of unmet need, including, but not limited to:

- Personalized medicines for certain subpopulations;
- Progress against rare and hard-to-treat illnesses;
- Treatments that improve patient adherence and quality of life;
- Need for additional treatments in a therapeutic area, such as a curative treatment;
- Treatments that improve the health of underserved and vulnerable communities who face health disparities;
- Treatments that benefit multiple common comorbidities at once; and

[153] BRG. (2020). Measuring the Relative Size of the 340B Program: 2020 Update. Available at: https://media.thinkbrg.com/wp-content/uploads/2022/06/30124832/BRG-340B-Measuring-Relative-Size-2022.pdf
[154] Conti RM, Bach PB. (2013). Cost consequences of the 340B drug discount program. JAMA. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4036617/.
[155] FDA. (2014). Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. Available at: https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf.
[156] Chambers, J.D., Thorat, T., Wilkinson, C. L., Neumann, P. J. (2017). Drugs Cleared Through The FDA's Expedited Review Offer Greater Gains Than Drugs Approved By Conventional Process. Health Affairs;36(8):1408-1415. DOI: 10.1377/hlthaff.2016.1541.

- The stepwise nature of progress in which significant gains for patients are achieved via advances that build on one another.

Additionally, ***PhRMA recommends that CMS consider unmet need across the product lifecycle***. The drugs selected by CMS will not be new to the market – although they may have met an unmet need at some point in their lifecycle, it is possible and even likely that treatment options will have changed by the time they are selected for the Program. This includes selected drugs that received expedited review by the FDA, which as noted above has an established definition of unmet need. Moreover, CMS' consideration of whether a drug meets an unmet need after its initial FDA approval is important to preserve incentives for post-approval research, as previously discussed.

g. Therapeutic Advance

Section 1194(e)(2)(A) requires CMS to consider "[t]he extent to which such drug represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives." Similar to our above comments on unmet need, it is critical that CMS acknowledge, in setting MFPs, medicines that represent an advance over existing treatments to maintain incentives for ongoing biopharmaceutical innovation. For drugs that represent a significant therapeutic advance, CMS should strongly consider setting MFPs at the statutory ceiling price.

Fortunately, CMS has both references within existing reimbursement policy, as well as resources, that can assist in defining and assessing selected drugs against this criterion. Furthermore, relying on existing Medicare policy would grant manufacturers of selected drugs critical predictability in understanding the criteria they must meet in order to obtain the statutory ceiling price for selected drugs.

One of these references is the New Technology Add-On Payment (NTAP) designation, which exists to ensure adequate reimbursement for certain new products that demonstrate, among other things, enhanced clinical improvement over existing technologies. In order to receive an NTAP, a product must demonstrate a substantial clinical improvement over existing services or technologies (in addition to two other distinct criteria), which is defined as "an advance that substantially improves, relative to…technologies previously available, the diagnosis or treatment of Medicare beneficiaries." A product meets the substantial clinical improvement criterion for an NTAP if it satisfies one of the following factors:

- "The new…technology offers a treatment option for a patient population unresponsive to, or ineligible for, currently available treatments.
- The new…technology offers the ability to diagnose a medical condition in a patient population where that medical condition is currently undetectable or offers the ability to diagnose a medical condition earlier in a patient population than allowed by currently available methods and there must also be evidence that the use of the new…technology to make a diagnosis affects the management of the patient.
- The use of the new…technology significantly improves clinical outcomes relative to services or technologies previously available…
- The totality of the information otherwise demonstrates that the new…technology substantially improves, relative to technologies previously available, the diagnosis or treatment of Medicare beneficiaries."[157]

[157] 42 CFR § 412.87(b)(1)(ii) "Additional payment for new medical services and technologies: General provisions."

The NTAP definition for substantial clinical improvement represents an established measurement that has been used for evaluating the value of certain products. By relying on an existing definition already in use in the Medicare program, CMS would be able to build on internal processes, experience and expertise used by the Agency to assess products that have applied for an NTAP. ***PhRMA recommends that CMS deem any drug that meets or has met the NTAP definition of "substantial clinical improvement" as representing a significant therapeutic advance and set the MFP at the ceiling price.*** This would not only apply to drugs that received official NTAP status previously, but any drug that currently meets the definition of "substantial clinical improvement" should be deemed as representing a therapeutic advance and should receive the ceiling price.

Additionally, PhRMA believes that highly credible, physician-driven oncology compendia, which CMS already relies on in other contexts, are important reference points for determining whether a treatment represents a therapeutic advance. Since 2008, the National Comprehensive Cancer Network (NCCN)'s Drug and Biologics Compendium has been one of these trusted resources. The NCCN Compendium's aim is to provide stakeholders, including policymakers with information to "improve the effectiveness and quality of care for patients by developing and disseminating up-to-date, authoritative information."[158] The recommendations in the Compendium are driven by stakeholders who should be central to the process for determining MFPs – multidisciplinary expert panels representing different specialties, including clinicians and patient advocates. Importantly, the Compendium is also updated on a regular basis to reflect currently available evidence.

Within the NCCN Compendium, indicated uses are categorized in a systematic approach that describes the type of evidence available for and the degree of consensus underlying each recommendation. NCCN considers evidence of both efficacy, safety of interventions, as well as an intervention's toxicity. The two highest potential recommendation categories (of four) and their definitions are:

- Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate; and
- Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[159]

These two levels of recommendations reflect that a treatment is supported by strong evidence, as well as near uniform consensus (a majority vote of at least 85 percent of the expert panel) among experts that the intervention is appropriate for the listed indication. Given the consensus this designation reflects, and its credibility, ***PhRMA recommends that CMS deem any oncology drug receiving a Category 1 or 2A rating as a significant therapeutic advance and set MFPs for drugs that receive these designations in the Compendium at the ceiling price.***

h. Manufacturer Engagement

In the Guidance, CMS states that if the Primary Manufacturer does not accept CMS' written initial offer and proposes a written counteroffer, which is subsequently not accepted by CMS, the Agency will invite the Primary Manufacturer to an in-person or virtual meeting that would take place within 30 days of CMS' receipt of the Primary Manufacturer's written counteroffer. After this initial meeting, each party would have the opportunity to request one additional meeting, for a maximum of three meetings between CMS and the Primary Manufacturer. In addition, all meetings must occur during a narrow time period – approximately four months' time between the Primary Manufacturer's written counteroffer to CMS and the end of the price setting period.

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[158] National Comprehensive Cancer Network. (2008). "Submission Request to CMS." Available at: https://www.cms.gov/Medicare/Coverage/CoverageGenInfo/downloads/covdoc14.pdf.
[159] National Comprehensive Cancer Network. "Definitions for NCCN Categories." Available at: https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines.

While PhRMA appreciates CMS' willingness to provide some opportunities for manufacturer engagement, we believe that, in addition to the described meetings during the offer and counteroffer process, manufacturers should be permitted to engage with CMS much earlier in the process and should not have to wait until after an offer and counteroffer are rejected to meet with the Agency. PhRMA believes that CMS should meet with manufacturers at key decision points in the MFP process, similar to the opportunities for engagement that FDA provides manufacturers during the drug review and approval process. The purpose of the meetings would include providing an opportunity for a dialogue where CMS and manufacturers could ask questions of one another, including questions about the data CMS evaluates to determine a selected drug's MFP and allowing manufacturers to provide context and correct errors regarding the data that CMS relies on to set the MFP, including data given to CMS by third parties.

Specifically, ***PhRMA recommends that CMS offer manufacturers the opportunity to meet[160] with relevant Agency staff at least three times prior to a counteroffer, including:***

- After drug selection but prior to initiation of the price setting process, to permit the manufacturer to provide critical input on issues such as potential evidence sources and comparator choice;
- Prior to CMS presenting the initial offer, so that CMS can provide information on its decision-making, analysis it conducted, and evidence sources, and permit the manufacturers to correct errors and provide important context; and
- After CMS presents the initial offer, so that manufacturers have the ability to discuss the data and assumptions that informed the initial offer.

The process that CMS proposes – whereby manufacturers would meet with CMS only after an initial offer and counteroffer are rejected, with all meetings forced into a four-month period – is insufficient and does not provide an opportunity for meaningful dialogue. While PhRMA reiterates that the Program cannot be thought of as a true negotiation, if CMS genuinely wants both a dialogue with manufacturers and a scientifically robust analysis of the clinical benefits of the selected drug, it should establish a process with sufficient time to meet and exchange information.

i. Patient and Clinician Engagement

CMS fails to outline a clear and meaningful process to engage with key stakeholders. Throughout the 91-page Guidance, there is barely any mention of the role of clinicians and patients as critically important stakeholders. The only formal opportunity for outside parties' input is through a generic ICR with a very short (30-day) deadline for input that begins after the list of selected drugs is published. PhRMA believes that providing clinicians and patients with only this limited role is a damaging misstep and lost opportunity that will significantly undermine the strength and reliability of the Program.

PhRMA strongly recommends that CMS develop a comprehensive and deliberative process to solicit input and advice from stakeholders, particularly patients, clinicians, and caregivers, at the start of the price setting process so they may provide relevant information to CMS in a timely manner. Patients[161] and clinicians bring unique and essential expertise and perspectives on the value of medicines. Their firsthand experience with selected drugs in a real-world setting will likely lead them to develop perspectives that differ significantly from the perspectives of

[160] The definition of a "meeting" should be established by CMS. The FDA meeting criteria and tiering approach might be applicable for CMS. Please See: US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER). Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products: Guidance for Industry. (DRAFT GUIDANCE). December 2017, Procedural.

[161] CMS should define "patients" broadly in this process and seek input from patients and family caregivers with lived experience with a specific disease state or therapeutic area, but also stakeholders who may not have that experience but who serve as patient advocates or are experts in issues such as health equity.

researchers assessing a treatment's value. The importance of including patient and clinician input in evidence-based processes has been underscored by a wide range of academics, thought-leaders, and research organizations. For example, in publishing its Rubric for patient-engagement, PCORI stated: "Engaging patients, caregivers, and other health care stakeholders as partners in planning, conducting, and disseminating research is a promising way to improve clinical decision-making and outcomes."[162]

CMS recently published an ICR that includes "optional" submissions of data from Primary Manufacturers and the public regarding evidence about alternative treatments described in section 1194(e)(2).[163] Such information would need to be submitted no later than 30 days after publication of the selected drug publication list, would follow the questionnaire format of CMS' ICR, and would be in written format only. PhRMA is concerned that this regimented process will not be well-publicized or accessible to patient or clinician groups, when such input is essential to the MFP process. It is imperative that CMS gain relevant input early in the process and meaningfully consider it in determining specific MFPs. As previously noted, PhRMA also recommends that prior to making its initial offer to the manufacturer, CMS make available to the public key elements of its MFP analysis and provide an opportunity for the public to comment on them.

Clinician input will be particularly important for CMS to ensure that decision-making is rooted in the clinical reality of how selected drugs are used in a real-world clinical practice, and the drugs' impact on patients. CMS should specifically solicit advice from clinicians with experience specific to the relevant therapeutic area or disease state (e.g., if a treatment for Parkinson's disease is evaluated, a neurologist who specializes in Parkinson's disease or movement disorders should be consulted). Recent research found that estimates of value corresponding to assumptions identified by clinician-researcher experts and ICER often differed by substantial margins when examining the value of poly (ADP-ribose) polymerase (PARP) inhibitors in ovarian cancer. The differences found had a significant impact on results – utility estimates and treatment duration estimates yielded notable differences in the estimated value of the treatments.[164]

These differences extend to assessments of a treatment's benefit compared to therapeutic alternative(s). A recently released study found that physicians in the U.S. disagreed with the German health agency's determination of the clinical benefit of innovative diabetes medicines 89 percent of the time. Of the U.S. physicians that disagreed, 97 percent said that the drugs in question provided additional clinical benefit for patients.[165] By including input from patients and relevant clinicians, CMS can help avoid discrepancies between how insurers or other price-setting agencies evaluate medicines versus how patients and clinicians value such medicines.

PhRMA recommends CMS consult with clinical leaders of the appropriate medical specialty societies, as well as leading clinical experts, during implementation of the Program and throughout the MFP determination process. This would include, at a minimum, key milestones, such as the scoping process for CMS' analysis, before the Agency makes an initial offer, and, if needed, in responding to a potential manufacturer counteroffer.

CMS has several options to facilitate input from clinicians in informal and formal manners. For example, CMS could convene ad hoc groups of clinicians and patients. In addition, CMS could establish a standing committee that provides input/recommendations, similar to the existing relationship between CMS and the American Medical Association (AMA), RVS Update Committee (RUC) or the Physician-Focused Payment Model

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[162] Sheridan S, Schrandt S, Forsythe L, Hilliard TS, Paez KA; Advisory Panel on Patient Engagement (2013 inaugural panel). (2017). The PCORI Engagement Rubric: Promising Practices for Partnering in Research. Ann Fam Med;15(2):165-170. DOI: 10.1370/afm.2042. PMID: 28289118; PMCID: PMC5348236.
[163] 54 Fed. Reg. 16983 (March 21, 2023).
[164] Cohen, J. T., Olchanski, N., Ollendorf, D. A., Neumann, P. J. (2022). The Certainty of Uncertainty in Health Technology Assessment. Health Affairs Forefront. Available at: https://www.healthaffairs.org/do/10.1377/forefront.20220125.37540/.
[165] NAVLIN Insights. (2019). U.S. physicians disagree with Germany's determinations of the value of diabetes medicines. Eversana. Available at: https://www.eversana.com/insights/u-s-physicians-disagree-with-germanys/.

Technical Advisory Committee (PTAC).[166] Alternatively, particularly given the short timeframe before the first drugs are selected for price setting, CMS could also consider engaging an existing advisory committee, such as the Medicare Evidence Development and Coverage Advisory Committee (MEDCAC), as a resource in the MFP process.[167]

Finally, following the statutorily required publication of the MFP explanation, PhRMA recommends CMS solicit feedback from all stakeholders regarding whether CMS has appropriately evaluated available evidence and arrived at an appropriate conclusion. This process will require CMS to ensure that the explanation provided after finalization of the MFP provides sufficient insight into CMS' decision-making process so that stakeholders are able to provide constructive and meaningful feedback.

j. Initial Justification

The written initial offer from CMS, which must be made no later than February 1st, 2024, must include a "concise" justification for the offer based on the negotiation factors and the methodology CMS lays out for developing an initial offer. The initial offer's justification is a critical part in the price setting process, particularly given the lack of communication between the manufacturer of the selected drug and the Agency that exists under CMS' proposed process. CMS must ensure that the initial justification enables the Primary Manufacturer to better understand the context for CMS' MFP offer, to inform the counteroffer and data provided as part of the counteroffer. As such, CMS needs to disclose all inputs and methodologies that it uses to arrive at an initial offer and must share this information prior to making the initial offer to ensure the manufacturer can properly respond to CMS.

PhRMA recommends that CMS describe, in final guidance, the template it will use for the concise justification and that it include information similar to the final published explanation and identify key pieces of information including:

- ***Therapeutic alternative(s) for a selected drug (for each indication);***
- ***How each of the factors listed in section 1194(e) were weighed relative to one another in CMS' decision-making;***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties CMS engaged formally or informally;***
- ***Benefits and impacts of a selected drug CMS considered; and***
- ***Stakeholders, and other government agencies and organizations CMS engaged, formally or informally, including how stakeholder input explicitly informed CMS' determination of the MFP.***

k. Explanation for the MFP

CMS states that it will publish an explanation for the MFP no later than March 1st of the year prior to the IPAY year. For example, CMS will provide an explanation for the MFP for IPAY 2026 on March 1st, 2025. The intent of the published explanation is to summarize how the relevant factors were considered during the price setting process and would focus on the factors that had the greatest influence in determining the MFP. The published

[166] The RUC is a volunteer group of 32 physicians and other health care professionals who advise CMS regarding the valuation of a physician's "work" under the Medicare physician fee schedule. The PTAC is an 11-member group that provides comments and recommendations to the HHS Secretary on physician payment models.

[167] This advisory committee provides independent guidance and expert advice to CMS on specific clinical topics. MEDCAC is used to supplement CMS' internal expertise and has experience reviewing medical literature and technology assessments. The MEDCAC includes clinicians and patient advocates and could be a useful forum for CMS to convene in establishing the Program. CMS notes that it may recruit non-MEDCAC members who have relevant expertise to provide additional input to Committee members.

explanation will include high-level comments on the submitted data, without any proprietary information. The published explanation will list the selected drug, discuss contributing price setting factors, and note any factors or circumstances that may be unique to the selected drug. If the MFP is not agreed upon, CMS will indicate that no Agreement was reached.

PhRMA notes that for IPAY 2027, "Primary Manufacturers" will be required to submit manufacturer-specific data to CMS by March 1st, 2025, on the very same date such manufacturers have access to the explanation for how CMS arrived at the MFP for the prior year. This is an unworkable timeline. ***PhRMA strongly recommends that the MFP explanation be released simultaneously with the MFP and before the process to set prices for IPAY 2027 begins*** in order to give manufacturers essential predictability in CMS' decision-making process. Manufacturers can better understand the process if they have access to the MFP explanation prior to being required to submit data to CMS for the following year. The statute requires CMS to publish the explanation *no later than* March 1st of the year prior to the IPAY, which indicates that CMS has discretion to publish the explanation at an earlier date. The published explanation of the MFP should be an important chance for CMS to solicit stakeholder feedback to improve the price setting process and is a critical piece in helping stakeholders understand how CMS arrives at an MFP for a selected drug. As this explanation could help build trust between CMS and other key stakeholders, ***PhRMA recommends the explanation provide information on many of the issues previously addressed, including but not limited to:***

- ***Therapeutic alternative(s) for a selected drug (for each indication);***
- ***How each of the factors listed in section 1194(e) were weighed relative to one another in CMS' decision-making;***
- ***Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties engaged formally or informally by CMS;***
- ***Benefits and impacts of a selected drug CMS considered; and***
- ***Stakeholders and other government agencies and organizations CMS engaged, formally or informally, including how stakeholder input explicitly informed CMS' determination of the MFP.***

As noted above, PhRMA also recommends that CMS offer manufacturers an opportunity to comment on a draft MFP explanation and that CMS respond to such comments.

l. Average Non-FAMP (Section 60.2.3)

Calculation of 2021 Annual non-FAMP

In section 60.2.3 of the Guidance,[168] CMS states that, in calculating the average 2021 non-FAMP for a selected drug, CMS intends to use the non-FAMP of each NDC-11 for the selected drug for each quarter of calendar year 2021. ***For the reasons discussed below, PhRMA instead recommends CMS to use the annual non-FAMP already reported by manufacturers to the VA as defined in 38 U.S.C. § 8126(h)(5).*** Specifically, for 2021, this would be the annual non-FAMP value reported by manufacturers to the VA by November 15, 2021.

In defining the average non-FAMP, the IRA does not specify which four quarters are "the 4 calendar quarters of the year involved" but notably cross-references 38 U.S.C. § 8126(h)(5). As noted above, 38 U.S.C. § 8126(h)(5) already defines an annual non-FAMP as a weighted average across the four quarters of the federal fiscal year, which runs from October through September of the following year. In defining the average non-FAMP for purposes of the IRA as based on a calendar year, CMS is introducing confusion, inefficiency, and added burden

[168] This approach is also proposed in section 60.2.1 with reference in section 50.1.

on both manufacturers and the Agency itself. Given the statutory reference to 38 U.S.C. § 8126(h)(5), CMS should instead utilize the existing annual non-FAMP as reported to the VA.

If CMS finalizes this portion of the guidance with the continued use of calendar year quarters, PhRMA supports the Agency's proposal for a weighted average.

Clarifying Weighting in Calculating a Single Average non-FAMP

In section 60.2.3 of the Guidance, CMS addresses its intended approach for calculating a single average non-FAMP across dosage forms and strengths of a selected drug for comparison against the calculated sum of the plan specific enrollment weighted amounts for the selected drug.

As written, the language included in the Guidance for steps 1 through 11 of section 60.2.3 could be read as utilizing units of NDC-11s used in the calculation of non-FAMP or units sold across all markets as opposed to units dispensed within the Part D program, which would result in an inconsistency with sections 60.2.2. and 60.5.

PhRMA urges CMS to clarify that the calculation of a single non-FAMP across dosage forms and strengths will be weighted by the 30-day equivalent supply dispensed under the Part D program as reported on the PDE. This would align the weighting methodology for the non-FAMP calculations with the weighting by 30-day equivalent supply utilized by CMS for the calculation of plan-specific enrollment weighted amounts in section 60.2.2 and the application of the single MFP across dosage forms and strengths in section 60.5.

Cross-Walking non-FAMP and PDE Unit Types

In step one of the calculation laid out in section 60.2.3 of the Guidance, CMS notes that the non-FAMP unit type may differ from unit types used on the Part D PDE record, which uses NCPDP-defined values. In such cases, CMS proposes to convert the non-FAMP unit type to the PDE unit type such that the average non-FAMP and the sum of plan specific enrollment weighted amounts represent the same quantity of the selected drug.

PhRMA agrees with the Agency on the need to convert non-FAMP units to PDE units in cases where the unit types differ for the same medicine. We would also encourage CMS to add a field to the PDE file layout to collect how the amount reported in the "Quantity Dispensed" field is measured using the NCPDP-defined values, as the Agency proposed in the Part D inflation rebate Guidance issued earlier this year.[169] Having this field added to the PDE would help CMS ensure accurate conversion of non-FAMP to PDE units, just as the Agency noted the potential of this field in helping to ensure accurate conversion of PDE to AMP units in the Part D inflation rebate Guidance.

m. Application of the MFP Across Dosage Forms and Strengths (Section 60.5)

In section 60.5 of the Guidance, CMS provides its intended approach to applying a single MFP across each dosage form and strength of a selected drug in accordance with section 1196(a)(2) of the Act. A key piece of this proposed approach (and indeed, a key piece of the methodologies CMS lays out in sections 60.2.2, 60.2.3, and 60.3 as well) rests on defining 30-day equivalent supplies for each dosage form and strength of a selected drug and therapeutic alternative(s).

PhRMA urges CMS to provide greater clarity regarding how the Agency intends to calculate 30-day equivalent supplies and identify alternative(s) when a 30-day supply cannot provide a reasonable comparison between therapeutic alternative(s). This calculation may not be as straightforward as it appears, particularly for certain types of medicines. Take the following two examples where CMS should give additional consideration to how to

[169] CMS. (February 9, 2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of SSA, and Solicitation of Comments. Available at: https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf

appropriately calculate 30-day equivalent supplies: (1) medicines used on an as-needed basis, such as rescue inhalers; or (2) when comparing two products where the treatment duration varies significantly (e.g., an oncology medicine that is administered on an ongoing basis until disease progression vs. a fixed-dose therapy) comparing the cost of a 30-day equivalent supply would not accurately capture the total cost of comparable outcomes. Medications where 30-day supplies can vary significantly across patients also need to be accounted for. For example, among patients using insulin, a typical 30-day supply can be very different from one patient to the next, both because different patients need different amounts of insulin, but also because insulin dosing varies by indication (e.g., for treatment for Type I vs. Type II diabetes). CMS should also give careful thought to how best account for starting dosages of medicines, where a patient's dosage increases over a period of time upon first starting a medication before reaching a steady, long-term dosage amount (e.g., titration).

PhRMA notes that manufacturers have experience with calculating 30-day equivalent supplies under certain state drug price transparency reporting requirements, and there are certain vendors that assist manufacturers with these calculations.[170] We suggest that CMS speak with manufacturers and these vendors to better understand how 30-day equivalent supplies are calculated for medicines, particularly medicines falling into one of the more complicated situations described in the paragraph above.

In addition to providing clarity on how the Agency intends to calculate 30-day equivalent supplies, PhRMA urges CMS to provide insight and data to manufacturers such that manufacturers can fully understand the Agency's application of a single MFP across dosage forms and strengths. Specifically, PhRMA requests that CMS make available to manufacturers of selected drugs:

- The Agency's calculated 30-day equivalent supply for each NDC-9;
- The total number of units dispensed for each NDC-9 in the 2022 Part D PDE data; and
- An Excel template with the Agency's 10-step calculation approach for applying the MFP across different dosage forms and strengths.

In providing this information to manufacturers of selected drugs, CMS will help to ensure that manufacturers have full transparency into the Agency's calculations.

n. Dispute Resolution

We are disappointed that CMS does not discuss mechanisms for dispute resolution, particularly after the Agency had indicated in its January 11, 2023 memo that "dispute resolution process for specific issues that are not exempt from administrative or judicial review under section 1198" would be one of seven major issues discussed in the Guidance.[171] While the Agency references this in the introduction to the Guidance, it does not then describe any policy for resolving disputes or affording opportunities for manufacturers to engage with CMS to correct errors. Despite appeals mechanisms being widely recognized as a "best practice" for HTA-informed policy decision-making, CMS appears to be taking the position that provisions in SSA section 1198 preclude administrative and judicial review for many of the basic elements of the MFP program. PhRMA disagrees with any such interpretation of section 1198. Specifically, section 1198 does not prohibit CMS from establishing informal procedures to resolve disputes and affording manufacturers the opportunity to engage with the Agency to correct errors that will inevitably arise during the MFP decision-making process. Indeed, CMS interpreted similar statutory provisions on administrative and judicial review in connection with the Part B and Part D inflation

[170] For example, Global Pricing Innovations (https://globalpricing.com/).
[171] CMS. (Jan. 11, 2023). Medicare Drug Price Negotiation Program: Next Steps on Implementation for Initial Price Applicability Year 2026. Available at: https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf.

rebates to accommodate an error correction process.[172] We were disappointed CMS chose not to put this discretion to use in the service of good public policy, as these opportunities to engage in meaningful dialogue to resolve disputes and correct errors would benefit both manufacturers and CMS and, importantly, could help avoid implementation missteps.[173] We encourage CMS to incorporate these processes into its final guidance for IPAY 2026.

Because the MFP program will involve CMS gathering and evaluating extensive and disparate types of cost and clinical data and research, and applying them to national MFP pricing decisions, it will create numerous potential areas where errors can occur or disputes arise over valid, but differing, assumptions (for example, interpretations on the appropriate approach to synthesizing data from different studies, or assumptions or extrapolations of treatment benefit based on study results). The risk of errors and disputes occurring will be further enhanced because the Agency will be required to conduct extensive evidence reviews in a much shorter time period than is typically required for traditional systematic reviews.[174]

IV. Removal from the Selected Drug List Before or During Negotiation, or After an MFP is in Effect (Section 70)

For purposes of a selected drug's exit from the Program, "CMS will consider an approved generic drug or licensed biosimilar biological product to be marketed when [PDE] data reveal that the manufacturer of the generic drug or biosimilar biological product has engaged in bona fide marketing of that drug or product." As discussed in greater detail in our comments on section 90 below, there is no statutory basis for CMS' proposed "bona fide marketing" standard. Nevertheless, however CMS defines "marketing," CMS' timeline in section 70 for removing a selected drug is overly restrictive.

Specifically, CMS could read the law to allow a reference product to exit the Program if a generic or biosimilar product is marketed after the "negotiation period" but before the IPAY begins. Such reading aligns with the statutory definition of a (QSSD)—a threshold requirement for a drug to be subject to price setting. The statute defines a QSSD "with respect to an initial price applicability year,"[175] indicating that a product's status as a QSSD must exist as of the first day of the IPAY, not just at the selected drug publication date, as the Guidance suggests. Had Congress intended QSSD status to be assessed only as of the selected drug publication date, it would have said so. Thus, a product that has become multisource before the IPAY should not be subjected to price setting. This view also comports with the definition of "price applicability period," which means, "*with respect to a qualifying single source drug*, the period beginning with the first initial price applicability year with respect to which such drug is a selected drug and ending with the last year during which the drug is a selected drug."[176] This reference to QSSD status signals that a product that has gone multisource and hence no longer meets the QSSD definition should not be subject to a price applicability period. Moreover, as the statute and CMS' Figure 1 in the

[172] CMS. (Feb. 9, 2023). Medicare Part B Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1847A(i) of the Social Security Act, and Solicitation of Comments. Available at: https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf; Available at: https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf CMS. (Feb. 9, 2023). Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of section 1860D-14B of the Social Security Act, and Solicitation of Comments. Available at: https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf.

[173] Kelly, C. (2023). Medicare Price Inflation Rebate List Revisions a Sign of IRA Implementation Overload? Pink Sheet. Available at: https://pink.pharmaintelligence.informa.com/PS148020/Medicare-Price-Inflation-Rebate-List-Revisions-A-Sign-Of-IRA-Implementation-Overload?vid=Pharma.

[174] New York University Health Sciences Library. (2023). Systematic Reviews. NYU Langone Health. Available at: https://hslguides.med.nyu.edu/systematicreviews/process.

[175] SSA § 1192(e)(1).

[176] SSA § 1191(b)(2) (emphasis added).

Guidance show, only products that are QSSDs may be eligible drugs. Where a product is no longer a QSSD, it cannot, by definition, be considered an eligible drug or a selected drug.[177]

Our position aligns with subsection (c)(1) in section 1192 and its use of the phrases, "with respect to the [IPAY]" and "with respect to such year" in paragraph (1).[178] This phrasing supports the conclusion that eligibility status (and hence, QSSD status) must remain in place as of January 1 of the IPAY for subsection (c)(1) to apply to the drug. Thus, this provision speaks to the exit process for drugs that remain a QSSD and selected drug on the first day of the IPAY and then experience generic or biosimilar competition. Paragraph (2) "clarif[es] the application of paragraph (1) to a specific time period when various tasks otherwise would need to be performed by both CMS and the manufacturer, i.e., during the negotiation period. The provision does not address what happens if the generic or biosimilar is marketed after the negotiation period, as there is no "negotiation process" to which the manufacturer is subject, and thus no need for a clarification that the process must stop. Paragraph (2)'s styling as a "clarification" shows that the underlying defined statutory terms referenced in subsection (c) must be given full effect in subsection (c)(1). In other words, it does not change the fact that the statute defines QSSD "with respect to an [IPAY]."

This position is grounded in sound policy. Congress crafted the IRA to provide for price setting for *single source* products. CMS' current position undermines this intent by applying MFPs to products that are already multisource. This position thereby directly undermines generic and biosimilar competition and incentives for pursuing approval of these products. For generic and biosimilar companies, developing and marketing generic and biosimilar products within the timeframes under the law is already challenging. The processes necessary to market a generic or biosimilar product can be complex, and there are many steps that are not solely in control of the generic or biosimilar sponsor, including FDA review timelines. The MFP may go into effect before they are ever able to market their products and may set a price below the level of economic viability. CMS' position compounds this problem by essentially providing that generic or biosimilar marketing in the last thirteen months before the IPAY does not trigger Program exit. In other words, a generic or biosimilar company that bring their products to the market during these thirteen months will nevertheless be forced to compete with an MFP.

We therefore urge CMS to revise the Guidance to provide that a reference product or listed drug exits the Program if generic or biosimilar marketing occurs after the negotiation period but before the IPAY. CMS also should amend the table on page 63 of the Guidance as follows.

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[177] SSA § 1192(c) (defining "selected drug"), 1192(d) (defining "negotiation-eligible drug").

[178] The section provides as follows:

> (c) SELECTED DRUG.—
> (1) IN GENERAL.—For purposes of this part, in accordance with subsection (e)(2) and subject to paragraph (2), each negotiation-eligible drug included on the list published under subsection (a) with respect to an initial price applicability year shall be referred to as a 'selected drug' with respect to such year and each subsequent year beginning before the first year that begins at least 9 months after the date on which the Secretary determines at least one drug or biological product—
> (A) is approved or licensed (as applicable)—
> (i) under section 505(j) of the Federal Food, Drug, and Cosmetic Act using such drug as the listed drug; or
> (ii) under section 351(k) of the Public Health Service Act using such drug as the reference product; and
> (B) is marketed pursuant to such approval or licensure.
> (2) CLARIFICATION.—A negotiation-eligible drug—
> (A) that is included on the list published under subsection (a) with respect to an initial price applicability year; and
> (B) for which the Secretary makes a determination described in paragraph (1) before or during the negotiation period with respect to such initial price applicability year;
> shall not be subject to the negotiation process under section 1194 with respect to such negotiation period and shall continue to be considered a selected drug under this part with respect to the number of negotiation-eligible drugs published on the list under subsection (a) with respect to such initial price applicability year.

Date on which CMS determines that a generic drug or biosimilar biological product is approved and marketed	Result with respect to selected drug for the Program
September 1, 2023 through ~~August 1, 2024~~ December 31, 2025 (which includes Negotiation Period for initial price applicability year 2026)	Selected drug remains a selected drug for initial price applicability year 2026, though MFP does not apply; selected drug ceases to be a selected drug on January 1, 2027
~~August 2, 2024~~ January 1, 2026 through March 31, 2026	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026; selected drug ceases to be a selected drug on January 1, 2027.
April 1, 2026 through March 31, 2027	Selected drug remains a selected drug and MFP applies for initial price applicability year 2026 and calendar year 2027; selected drug ceases to be a selected drug on January 1, 2028.

V. Manufacturer Compliance and Oversight (Section 90)

a. Monitoring of Access to the MFP (Section 90.2)

Please refer to our comments on section 40.4 for a discussion of CMS' proposals in section 90.2 of the Guidance.

b. Monitoring for Bona Fide Marketing of Generic or Biosimilar Product (Section 90.4)

"Bona Fide Marketing"

With respect to section 90.4, even accepting for the sole purpose of commenting on this Guidance that CMS' adoption of a "bona fide marketing" standard is final, there is nevertheless no statutory basis for CMS' proposal "to monitor whether robust and meaningful competition exists in the market once it makes such a determination [that a generic drug or biosimilar biological product has been marketed]."[179] The statute contemplates that a selected drug will exit the program based on such a determination and nothing more, and does not provide CMS a role in monitoring generic and biosimilar competition. As set out below, CMS' concept of "bona fide marketing" is contrary to the statute. This approach also fails to provide clarity or certainty regarding when a medicine becomes ineligible for price setting.

The statute defines a QSSD in relevant part as a drug for which a generic or biosimilar product is not "marketed."[180] The guidance instead refers to a new term "bona fide marketing," providing that, "[i]n accordance with 1192(c) and (e) of the Act for the purpose of identifying [QSSDs] for [IPAY] 2026, CMS will review PDE data for a given generic drug or biosimilar . . . and will consider a generic drug or biosimilar biological product to be marketed when that data reveal that the manufacturer of that drug or product has engaged in bona fide

[179] Guidance, p. 67.
[180] SSA § 1192(e)(1)(A)(iii) & (B)(iii); *see also id.* § 1192(c)(1)(B) (addressing the termination of "selected drug" status following the Secretary's determination that a generic or biosimilar product "is marketed.").

marketing of that drug or product."[181] The addition of the term "bona fide" adds an extra-statutory limitation and is at odds with the ordinary meaning of "marketed."

Indeed, in the guidance's "Appendix C: Definitions for Purposes of Collecting Manufacturer-Specific Data," CMS defines "marketing" as "the introduction or delivery for introduction into interstate commerce of a drug product."[182] PhRMA agrees with this definition, which is consistent with FDA's interpretation of provisions of the FDCA for which a product's marketing status is relevant. For example, in the context of 180-day exclusivity for first generic applicants, the FDCA provides that FDA shall not make effective a subsequent generic application until "180 days after the date of the first commercial marketing of the drug…by any first applicant."[183] In regulations, FDA defines the term "commercial marketing" in relevant part as "the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant."[184] This definition is particularly relevant given that the IRA specifically refers to the generic product being "marketed under section 505(j) of the [FDCA]," which has long been understood to mean introduction into interstate commerce.[185] Had Congress intended to change the criteria for a generic to be considered "marketed," it would have done so. Similarly, for purposes of implementing section 506I of the FDCA concerning marketing status reports, FDA considers a product's marketing status to depend on whether a product is distributed by the application holder, i.e., whether the product is available for sale.[186] Notably, since the IRA's enactment, Congress extended the section 506I marketing provisions to apply to biologics licensed under the PHSA and in so doing made no changes that would suggest Congress meant to do anything other than endorse FDA's approach to defining marketing status.[187] FDA's definitions reflect the generally accepted ordinary meaning of the "marketing" of a pharmaceutical product, and, consequently, the meaning of "marketed" that Congress intended in the context of the IRA. Moreover, in a Supreme Court case involving a law that used the term "marketing," but left the term "undefined," the Court used "ordinary meaning" of "marketing."[188] Significantly, the Court held that "[m]arketing ordinarily refers to the act of holding property for sale with the activities preparatory thereto . . . and does not require that the promotional or merchandising activities connected with the selling be extensive."[189] In contrast, the guidance imposes an extra-statutory limitation on qualifying marketing that goes beyond its ordinary meaning. ***We urge CMS to abandon the new term "bona fide marketing" and rely instead on the definition of "marketing" in Appendix C.***

CMS' position also conflicts with another part of the Program statute at section 1192(f)(2)(D)(iv) which expressly prohibits manufacturers from receiving the biosimilars-based selection "pause" based on volume-limited arrangements. Specifically, section 1192(f)(2)(D)(iv) states that "[i]n no case shall the Secretary delay the inclusion of a biological product as a selected drug on the list published under subsection (a) if the Secretary determined that the manufacturer of the biosimilar…entered into any Agreement described in such paragraph with the manufacturer of the reference product…that…*restricts the quantity (either directly or indirectly)* of the biosimilar biological product that may be sold in the United States over a specified period of time."[190] Clearly, then, Congress knew how to impose volume-based requirements or limitations and did so in the very same section of the statute. Again, when "Congress includes particular language in one section of a statute but omits it in another section of the same Act," it is "generally presumed that Congress acts intentionally and purposely in the

[181] Guidance, p. 10.
[182] Guidance, p. 82.
[183] FDCA § 505(j)(5)(B)(iv)(I).
[184] 21 C.F.R. § 314.3.
[185] Id.
[186] *See* FDA, Guidance for Industry, *Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format*, at 3 (Aug. 2020) (describing the discontinuation of marketing a product as ceasing distribution); *see also* FDCA § 506I (describing reporting requirements relating to marketing status).
[187] Consolidated Appropriations Act, 2023, Pub. L. No. 117-328, § 3201 (2022).
[188] *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 187–88 (1995).
[189] *Id.* (emphasis added).
[190] SSA § 1192(f)(2)(D)(iv) (emphasis added).

disparate inclusion or exclusion."[191] Congress's decision not to qualify the term "marketed" demonstrates that CMS' additional "bona fide" limitation conflicts with the statute.

The use of specific PDE data and the time frame for such data, as described in the Guidance, are also at odds with the statutory language. The guidance states that "CMS will review PDE data for a given generic drug or biosimilar biological product during the 12-month period beginning August 16, 2022 and ending August 15, 2023, using PDE data available on August 16, 2023, and will consider a generic drug or biosimilar biological product when that data reveal that the manufacturer of that drug or product has engaged in bona fide marketing of that drug or product."[192] The statute does not instruct CMS to consider PDE data – either exclusively, or at all – in assessing marketing status and to ignore all other sources of marketing information. Thus, in accordance with the statute, the determination of whether a product is marketed, as that term is commonly understood, should not be based on PDE data.

PDE data are inappropriate as a benchmark to assess whether a generic or biosimilar is marketed. PDE data only reflect Part D claims: Part D plans are a subset of payors, which themselves are a subset of the biopharmaceutical marketplace, and a subset that would be expected to pay for a newly approved drug later than other segments of the marketplace. And in fact, Medicare Part D plans are "notably slower than commercial plans in coverage of first generics…For the 2021 Medicare Part D plan year, on average, only 21 percent of first generics that launched in 2020 were covered by plan formularies." An analysis by the Association for Accessible Medicines found that "it takes nearly three years before first generics are covered on more than half of Medicare Part D formularies," and even when covered, these drugs are less likely to be placed on generic tiers (meaning that the generic may be infrequently used and thus may not appear in any particular sample of PDE data even if it is covered by the Part D plan).[193] This delayed utilization pattern – even for first generics – is consistent with the fact that CMS allows Part D plans' Pharmacy and Therapeutics Committees a lengthy period to review new drugs and decide whether to place them on formulary.[194] In short, hinging a decision about when a new generic or biosimilar is "marketed" solely on records of Part D utilization is an arbitrary and irrational approach that inevitably will miss most of the evidence of marketing and determine an incorrect date for when marketing of the drug began.

Finally, any monitoring by CMS of the competitive landscape for pharmaceuticals would duplicate the existing efforts of the Federal Trade Commission (FTC), which has the statutory authority and expertise to perform this function. It is also unnecessary in light of FDA initiatives, including the Drug Competition Action Plan[195] and Biosimilars Action Plan,[196] which have focused on improving access to generic and biosimilar products in the U.S. Moreover, the FTC and FDA have also been working together on these issues, issuing joint statements and holding joint workshops, most recently focusing on competition for biologics and biosimilars.[197] CMS also lacks the expertise and resources to police marketplace competition issues. CMS' proposed monitoring of the status of competition in the marketplace therefore is unauthorized and unnecessary.

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[191] *Russello v. United States,* 464 U.S. 16, 23 (1983) (citations omitted).
[192] Guidance, p. 10.
[193] New Generics are Less Available in Medicare than Commercial Plans, AAM at 5-6. (July 2021). Available at: https://accessiblemeds.org/sites/default/files/2021-07/AAM-New-Generics-Are-Less-Available-in-Medicare-2021.pdf at 5, 6. See also Appendix at p. 10 (showing that generic uptake in Medicare dipped as low as 12 percent for generics launched in 2017).
[194] Medicare Prescription Drug Benefit Manual, chap. 6, section 301.5 (Part D plans' P&T committees should generally make a "reasonable effort" to review a newly-approved drug within 90 days and decide whether to add the drug to the plan formulary within 180 days, or provide a "clinical justification" if this timeframe is not met); section 30.2.5 (even for new drugs in the Part D six protected classes, plan P&T committees have 90 days to review the new drug and add it to the plan formulary).
[195] FDA Drug Competition Action Plan. Available at: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/fda-drug-competition-action-plan.
[196] FDA Biosimilars Action Plan: Balancing Competition and Innovation. Available at: https://www.fda.gov/media/114574/download.
[197] FDA and FTC Collaborate to Advance Competition in the Biologic Marketplace. Available at: https://www.fda.gov/news-events/fda-voices/fda-and-ftc-collaborate-advance-competition-biologic-marketplace.

VI. Civil Monetary Penalties (Section 100)

In section 100 of the Guidance, CMS addresses the civil monetary penalty (CMP) provisions set forth in section 1197 of the SSA (the Program-related CMPs) and briefly describes the "procedures" CMS intends to follow to impose these CMPs on manufacturers. Our comments reflect how we believe CMS can implement these CMPs in a manner that conforms to the statute, while affording reasonable and appropriate protections to manufacturers.

a. Notice-and-Comment Rulemaking on Program-Related CMPs

The extraordinary nature of Program-related CMPs demands notice-and-comment rulemaking. Section 1197 authorizes extraordinarily high CMP amounts. To our knowledge, the maximum CMP amount set forth in section 1197(d), which provides for a penalty equal to $100 million for each item of false information, is *by far* the highest CMP amount related to any federal health care enforcement regime. Moreover, the maximum CMP amount set forth in section 1197(a) is equal to 10 times the difference between the price the manufacturer charges and the MFP[198] – a strikingly large amount in comparison to the most common punitive fine recognized in American law (*i.e.*, treble damages). Further, the maximum CMP amount set forth in section 1197(c) of $1 million per day greatly exceeds other "per-day" CMP amounts in the SSA (such as the maximum $10,000 per day penalty in section 1927(b)(3)(C)(i) for the similar failure of a manufacturer to provide timely information relevant to Medicaid drug rebates).

These extraordinarily high penalties, by themselves, warrant notice-and-comment rulemaking prior to Agency implementation. When coupled with the complexity and novelty of the Program and the implementation challenges that will persist for at least the first few years, basic notions of fairness and due process require notice-and-comment rulemaking. PhRMA strongly urges CMS to complete this notice-and-comment process before seeking to impose any Program-related CMPs on a manufacturer. Such rulemaking should address the following issues, at a minimum:

- Clear and detailed procedures CMS intends to use to impose Program-related CMPs against selected drug manufacturers;
- The scope of a selected drug manufacturer's Program-related CMP liability with respect to acts and omissions of third parties, including independent actors in the pharmaceutical supply chain over which the manufacturer exercises little, if any, control; and
- Factors CMS will consider in assessing whether to seek a Program-related CMP and the amount of any such CMP.

We address each of these issues, in turn, below.

b. Combined Rulemaking on CMP Procedures

PhRMA urges CMS to implement IRA drug pricing-related CMP procedures through a single rulemaking and model such procedures after well-established precedents. Given the significant overlap between the CMP provisions in sections 1197 (governing the Program), 1847A(i)(7) (governing Part B rebatable drugs), and 1860D-14B(e) (governing Part D rebatable drugs) of the SSA, PhRMA urges CMS to undertake notice-and-comment rulemaking to implement a common set of procedures to govern these CMPs.[199] We note that proceeding through notice-and-comment rulemaking to implement procedures for these CMPs would be consistent with CMS'

[198] A similar penalty amount applies with respect to a manufacturer's failure to pay a rebate due in connection with the biosimilar delay provisions. *See* SSA § 1197(b).

[199] To clarify, CMS should codify separate regulatory provisions to address the circumstances under which a manufacturer could be subject to a CMP under: (1) the Program; (2) the Part B inflation rebate program, and (3) the Part D inflation rebate program. These separate regulatory provisions should cross-reference a single CMP appeals procedure that applies to all IRA drug pricing-related CMPs.

obligation under section 1871(a) of the SSA to issue regulations before establishing a substantive legal standard.[200]

In developing procedures to govern the imposition of CMPs, CMS should use well-established agency procedures as a model. Examples include the CMP procedures for Medicare Advantage organizations (MAOs) and Part D prescription drug plan sponsors (PDPs),[201] and the CMP procedures issued by the HHS OIG.[202] Each of these examples establishes clear and detailed procedures for the Agency to provide detailed notice of the basis of the CMP and for the regulated parties to, among other things, respond to CMP notices, request hearings before an administrative law judge (ALJ), and appeal ALJ decisions to the HHS Departmental Appeals Board before seeking review in the U.S. Court of Appeals.[203]

In addition, the CMP procedures should provide an opportunity for manufacturers to confer with the Agency prior to the imposition of CMPs. Even when regulations do not require it, it is customary for government agencies to issue pre-enforcement notification letters or pursue other informal means to give regulated parties an opportunity to respond before the Agency initiates formal proceedings, such as by issuing a CMP notice.[204] Engaging in pre-enforcement discussions with manufacturers would be beneficial to both manufacturers and CMS. This is particularly true because of the extraordinarily high CMP amounts at issue and the novelty and complexity of the Program, which is still being implemented. Both manufacturers and CMS will likely be working through implementation challenges, often fact-specific, for at least the first few years of the Program. Therefore, it is critical that CMS implement a process to informally engage with manufacturers through pre-enforcement communications before initiating formal CMP proceedings.

c. CMPs Due to Acts and Omissions of Third Parties

PhRMA urges CMS to not impose CMPs on drug manufacturers for acts and omissions of third parties over which manufacturers have little, if any, control. As reflected earlier in our comments, PhRMA strongly opposes CMS' intention to hold a Primary Manufacturer responsible for certain acts and omissions of a Secondary Manufacturer. PhRMA is deeply concerned that, under this framework, CMS could attempt to impose $1 million-per-day CMPs on a Primary Manufacturer for acts or omissions of a Secondary Manufacturer over which the Primary Manufacturer has little, if any, control.[205]

Similarly, CMS intends to hold Primary Manufacturers "ultimately" "responsib[le]" for ensuring access to the MFP, despite acknowledging that "[e]ach component of the pharmaceutical supply chain may have a role in making the MFP available to MFP-eligible individuals."[206] Here, too, manufacturers have very limited, if any, ability to influence the conduct of independent actors in the pharmaceutical supply chain. Notwithstanding these

[200] In any event, under section 1847A(i)(7) of the SSA, CMS is expressly required to issue regulations establishing procedures governing CMPs under the Medicare Part B inflation rebate program.
[201] 42 C.F.R. Part 422, Subparts O and T (CMP procedures for MAOs); 42 C.F.R. Part 423, Subparts O and T (parallel procedures for PDPs).
[202] 42 C.F.R. Parts 1003 and 1005.
[203] We note that the limitations on administrative and judicial review set forth in section 1198 of the SSA do not limit a manufacturer's right under section 1128A(e) of the SSA to seek judicial review of a determination by the Secretary to impose a CMP pursuant to section 1197.
[204] *See, e.g.*, OIG, Revisions to the OIG's Exclusion Authorities, 82 Fed. Reg. 4100, 4109 (Jan. 12, 2017) ("In practice, OIG also contacts potential subjects of section 1128(b)(7) exclusions, often through 'pre-demand letters' or other means to give defendants the opportunity to respond to OIG before formal proceedings are initiated."); 42 C.F.R. §§ 422.756, 423.756 (setting forth CMS' procedure for imposing intermediate sanctions on MAOs and PDPs, respectively, which provides for a written notice to the plan of CMS' proposed intermediate sanction and an opportunity for the plan to provide a written rebuttal within 10 days of receipt of CMS' notice).
[205] For example, it appears from the guidance that CMS believes it could impose $1 million-per-day CMPs on a Primary Manufacturer in the following instances: (1) a Secondary Manufacturer fails to make the MFP available to MFP-eligible individuals or specified dispensers, *see, e.g.*, Guidance at 26, 68-69; and (2) a Secondary Manufacturer fails to provide a Primary Manufacturer with required non-FAMP information for a selected drug that the Primary Manufacturer would be required to submit to CMS for purposes of the "negotiation," *see, e.g.*, Guidance, pp. 27-28, 69.
[206] Guidance, p. 65.

limitations, the Guidance suggests manufacturers could face CMPs equal to 10 times the difference between the net acquisition price and the MFP *for each unit* of a selected drug acquired at a price exceeding the MFP.[207]

PhRMA strongly opposes any interpretation of the statute that would seek to impose CMP liability on manufacturers of selected drugs due to the acts or omissions of any independent third party. Doing so would dramatically expand the scope of manufacturers' legal liability and disrupt the allocation of risk under numerous contractual arrangements between and among manufacturers and other entities spanning the pharmaceutical supply chain. Amending these contracts to account for CMS' policy change would require significant time and resources that CMS does not address in setting forth these new compliance expectations for manufacturers.

While PhRMA strongly opposes CMS' intention to shift legal risk to manufacturers in this manner, if CMS retains these policies in the final IPAY 2026 guidance, the Agency should *at a minimum* articulate a non-enforcement policy pursuant to which it will refrain from imposing CMPs on Primary Manufacturers under sections 1197(a) and 1197(c) for a reasonable time following issuance of the final guidance for IPAY 2026.[208] In addition, as discussed below, if CMS pursues CMPs against any Primary Manufacturer based on a third party's conduct, CMS should weigh the Primary Manufacturer's level of culpability to seek a low penalty.

d. CMS Explanation of Factors Used in Assessing CMPs

CMS should publicly explain the factors it will consider in assessing CMPs against manufacturers. As a threshold matter, the extraordinary maximum penalty amounts for the Program-related CMPs present serious concerns under the Excessive Fines Clause of the Eighth Amendment to the U.S. Constitution. While these amounts are set by statute, in seeking to impose a CMP on a manufacturer, CMS should consider whether a compromise penalty amount below the statutory amount is required to avoid this constitutional issue.[209]

Moreover, given the extraordinary range of potential penalty amounts under the statutory maximums, PhRMA strongly urges CMS to clearly explain, through notice-and-comment rulemaking, the factors it will consider and weigh in assessing whether to seek a Program-related CMP and the amount of any such CMP. CMS has clear statutory authority to exercise such discretion. Specifically, each Program-related CMP cross-references section 1128A of the SSA, which requires that, in determining the amount of any CMP, agencies must consider "the nature of claims and the circumstances under which they were presented, "…the degree of culpability, …[and] such other matters as justice may require."[210]

Factors CMS should consider as part of this rulemaking include, for example:

- the nature and circumstances of the manufacturer's conduct;
- the degree of the manufacturer's culpability, including, for example, whether the manufacturer took timely and appropriate corrective action;
- whether the manufacturer had knowledge of a violation of an applicable Program requirement;
- the clarity of existing guidance available to the manufacturer;

[207] Guidance, pp.64-65, 68.
[208] We note that there is precedent for this approach. For example, OIG proposed adopting a similar policy of enforcement discretion in its 2020 proposed rule on CMPs related to information blocking. *See* 85 Fed. Reg. 22979, 22985 (Apr. 24, 2020) ("We appreciate that information blocking is newly regulated conduct…The goal in exercising our enforcement discretion is to provide individuals and entities that are taking necessary steps to comply with the ONC Final Rule with time to do so while putting the industry on notice that penalties will apply to information blocking conduct within a reasonable time.").
[209] SSA § 1128A(f) authorizes agencies to "compromise" CMPs imposed on regulated parties.
[210] SSA § 1128A(d).

- efforts by the manufacturer to obtain clear guidance from CMS and/or another government Agency on a specific issue impacting the manufacturer's compliance with an applicable Program requirement;
- good faith efforts by the manufacturer to comply with applicable Program submission deadlines (*e.g.*, submission of information pursuant to section 1193(a)(4)), considering reasonable requests by the manufacturer that CMS extend such deadlines in appropriate circumstances; and
- the degree to which a manufacturer could exercise control over, or sought to address the conduct of, a third party on which a manufacturer relied in satisfying an applicable Program requirement.

CMS' discussion of how it will consider and weigh these factors should provide clear, detailed, and meaningful distinctions in penalty amounts to help manufacturers focus compliance efforts consistent with CMS priorities. In light of ongoing implementation of the Program, which will continue for at least a few years, CMS should construe the foregoing factors liberally in favor of manufacturers and in a manner that would not trigger a CMP. Such an approach is particularly appropriate where a manufacturer has engaged with CMS in good faith and can demonstrate that it has taken reasonable steps to comply with applicable Program requirements.

e. Threshold for Manufacturer CMP Liability

Program CMPs that require a manufacturer to act "knowingly" should apply only if the manufacturer had actual knowledge. Section 1197(c) of the SSA is the only CMP provision that requires a manufacturer to act "knowingly" for liability to attach. Specifically, a manufacturer must knowingly provide false information under certain procedures that apply in connection with the small biotech exception or the biosimilar delay provisions. A manufacturer that knowingly submits such information is subject to a CMP equal to $100 million for each item of false information.

Separately, in section 100.2 of the Guidance, CMS states that a manufacturer would be out of compliance with the requirement to submit information under section 1193(a)(4) of the SSA and subject to a CMP equal to $1 million per day of a violation under section 1197(c) if it knowingly submits false information required under the Agreement between the manufacturer and CMS.

CMS should not attempt to impose a CMP on a manufacturer under either of these provisions unless CMS can first demonstrate that the manufacturer had actual knowledge of a violation. Importantly, the term "knowingly" is not defined in Part E of Title XI of the SSA. Nor is the term defined in section 1128A of the SSA, which is incorporated by reference into the Program-related CMPs.[211] In the absence of a legally binding definition of "knowingly," CMS should interpret this term based on its plain meaning, which requires one to act "[w]ith knowledge; consciously; intelligently."[212] The extraordinary amounts of these CMPs further support interpreting "knowingly" in its most natural way to reserve such penalties for only truly knowing conduct. Accordingly, CMS should not seek to impose a CMP under either of these provisions unless CMS can first demonstrate that the manufacturer had actual knowledge of a violation.

VII. Part D Formulary Inclusion of Selected Drugs (Section 110)

In section 110 of the Guidance, CMS notes that "Medicare Part D plans shall include each covered Part D drug that is a selected drug on Part D formularies during Contract Year (CY) 2026 and all subsequent years for which the MFP of the selected drug is in effect during the price applicability period." PhRMA agrees with CMS that, per the statute, any drug that is a selected drug, for which the MFP is in effect, must be on all Part D formularies and widely available to beneficiaries in Medicare.

[211] The Program-related CMPs incorporate the definitions and all other procedural aspects of section 1128A. Only the substantive violations described in subsections (a) and (b) are not incorporated.
[212] Black's Law Dictionary, Knowingly, https://thelawdictionary.org/knowingly/ (accessed Mar. 26, 2023).

PhRMA also would like to note our concerns that price setting, layered on top of the significant changes in stakeholder liability from Part D redesign, will have significant impacts on the structure of Part D and could negatively impact patient access to medicines. Indeed, we believe that price setting will put the very nature of Part D's competitive system at risk. Negotiations between plans and manufacturers around formulary and benefit designs are foundational elements of Part D's current market-based system, which has delivered broad access for beneficiaries to a range of plans and treatment options since the program's inception. The Agency must tread carefully in implementing the IRA and setting prices for selected drugs so that these foundational program elements are not completely undermined and beneficiary access to medicines is not lost or hindered.

As described in more detail below, the price setting in the IRA will have impacts far beyond the drugs selected for IPAY 2026, extending to other therapeutic competitors in the class. To that end**, *PhRMA recommends that CMS' process for arriving at a final MFP for selected medicines should seek to minimize effects within therapeutic classes that would result in narrower formularies and fewer choices for patients. CMS should also be mindful and seek to limit the risk of perverse incentives that are more likely to result from MFPs set at levels well below the ceiling price.*** CMS should create sufficient safeguards to ensure that there is diversity across plan formularies to offer beneficiaries plan options that continue to meet their individual therapeutic needs. In practice, this calls for plan formularies that include both selected drugs and medicines that aren't subject to government price controls.

To illustrate these concerns, recent analysis by the Hayden Consulting Group of the impact of the IRA's government price setting provisions on the Part D program show that the market-based competitive conditions that have led to historical access for a broad array of treatments in Part D could be stifled.[213] Specifically, Hayden examines illustrative therapeutic classes where there is significant brand-to-brand competition today and evaluates changes in plan liability before and after implementation of the IRA, assuming that at least one competitor in the class is subject to price setting. To limit an increase in liability and mitigate risk, Hayden concludes that plans are likely to impose aggressive utilization management to limit market share for medicines that are not subject to price setting, and/or demand higher rebates for formulary access.[214] Hayden's analysis assumes that these formulary dynamics occur when the MFP is set at the ceiling price and notes the "magnitude of the MFP discount will be the greatest determinant of competitive dynamics in the market."[215] To the extent that CMS sets MFPs for selected drugs well below the ceiling these potential formulary dynamics could intensify further.

As the IRA is implemented, Part D's broad choice of medicines must be maintained. CMS' MFP process should have as a key goal expanded access to medicines for Medicare beneficiaries – including coverage, access, and affordability that is as good as or better than what is in place today – rather than more restrictions in coverage**.** To that end, ***PhRMA recommends that CMS review and update its formulary review standards*** to reflect the significant shift from the competitive environment that has been in place since the Part D program's inception to today, recognizing the IRA's major changes to the Part D benefit as a result of redesign and government price setting for a steadily growing number of medicines over time. ***PhRMA specifically recommends that CMS pay close attention to plans' tiering decisions, cost-sharing levels, patient out-of-pocket exposure, and utilization management protocols for both brand and generic medicines to ensure that plans do not over-emphasize low premiums at the expense of enrollees having high quality benefits that provide affordable access to medicines.***

Given major changes in the Part D program occurring in the coming years, Part D plans are also likely to expand upon current trends towards more formulary tiers and increase the number of medicines subject to maximum

[213] Hayden Consulting Group. (Oct 31, 2022). Government Price Negotiation & its Anticipated Impact on Contracting Dynamics in Medicare Part D. Available at: https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act.
[214] Hayden Consulting Group. (Nov 10, 2022). Government Price Negotiation & its Anticipated Impact on Contracting Dynamics in Medicare Part D. Available at: https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act-3.
[215] Hayden Consulting Group. (Dec 20, 2022). Inflation Reduction Act: Impact of the DNP & Future Dynamics, including Medicare Part B. Available at: https://www.haydencg.com/post/hcg-white-paper-series-the-inflation-reduction-act-4.

coinsurance requirements, continuing to stratify their formularies and increasing the number of medicines placed on non-preferred and specialty tiers. According to MedPAC's most recent report to Congress, in 2019 most Part D beneficiaries were enrolled in plans that utilized a five-tier formulary, including a specialty tier for medicines exceeding a certain cost threshold, and the use of coinsurance was widespread.[216] Additional formulary tiers can result in access burdens for patients, as Part D plan sponsors typically impose up to 33 percent coinsurance for medicines on the specialty tier, and coinsurance for non-preferred tier medicines can be as high as 40 to 50 percent.[217]

Patient out-of-pocket burdens are exacerbated by current practices of Part D plan sponsors to retain the substantial discounts and rebates negotiated with manufacturers, typically using rebate dollars to reduce premiums overall instead of lowering patient cost sharing on rebated medicines. Even if a Part D sponsor or its PBM has negotiated a rebate for a medicine, beneficiary coinsurance is typically based on a medicine's undiscounted list price. A recent analysis found that 92 percent of Part D beneficiaries' out-of-pocket spending is based on the list price rather than the discounted price their insurer gets.[218] For beneficiaries with coinsurance, failure to pass through rebates at the point-of-sale could manifest in disproportionately high out-of-pocket costs for non-selected drugs. This is because while selected drugs will have their coinsurance calculated as a percentage of the MFP price, coinsurance for competing non-selected drugs will continue to be based on the undiscounted price of the drug, even in cases when the manufacturer provides a substantial rebate. To address the out-of-pocket challenges caused by plans' and PBMs' failure to pass rebates directly to patients at the point-of-sale, ***PhRMA recommends that CMS redefine Part D negotiated price to take into account all manufacturer price concessions.***

PhRMA also recommends that CMS update its plan evaluation and oversight procedures and rigorously exercise its responsibility to enforce statutory non-discrimination requirements in Part D. Specifically, PhRMA urges CMS to conduct diligent formulary oversight to guard against increasingly aggressive utilization management restrictions or the narrowing of patient treatment options, including exclusion of medicines. In particular, CMS should increase transparency of the Agency's formulary review processes, reporting on CMS' oversight and outcomes of the formulary reviews outlined in the Part D Benefits Manual.[219] Since Part D's origination, plans have increasingly restricted access to medicines in Part D through tighter formularies, limiting the number of medicines covered for beneficiaries. Additionally, insurers use utilization management as a strategy to reduce their spending on covered medicines, which can have a negative impact on patient access. These insurance tactics, including prior authorization and fail first (also known as step therapy), may prevent or delay patients from accessing the medicines prescribed by their physicians. A recent report from GoodRx found that the average number of medicines covered by Part D that are subject to utilization management

[216] MedPAC. (March 2019). Report to the Congress: Medicare Payment Policy. Chapter 14. Available at: https://www.medpac.gov/wp-content/uploads/import_data/scrape_files/docs/default-source/reports/mar19_medpac_ch14_sec.pdf

[217] Cubanski J, Damico A, Neuman T. (May 2018). Medicare Part D in 2018: The Latest on Enrollment, Premiums and Cost-Sharing. Kaiser Family Foundation.

[218] PhRMA. (March 2021) "Trends in Out-of-Pocket Spending for Brand Medicines in Medicare Part D." Available at: https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/S-U/Trends-in-Out-of-Pocket-Spending-for-Brand-Medicines-in-Medicare-Part-D_FINAL-Update-May-21.pdf.

[219] Section 30.2.7 (Formulary Performance and Content Review) of the Part D benefits manual, outlines CMS' key formulary review concepts which include: review of tier placement to ensure the formulary doesn't discourage enrollment of certain beneficiaries, determining whether appropriate access is afforded to drugs or drug classes addressed in widely accepted treatment guidelines, availability of the most commonly prescribed drug classes for the Medicare population, and review of UM restrictions to ensure that use of these tools are consistent with industry best practices and identification of outliers. CMS should more clearly define these standards such as what it means for a formulary to provide "appropriate access" and for UM restrictions to be "consistent with industry best practices" or "outliers." Additionally, CMS should issue an annual report providing aggregate data on the analyses it conducted, the results of those analyses, and changes to formularies and UM required by its analyses. Reporting should be sufficiently specific to allow stakeholders and researchers to assess the impact of CMS' formulary review on formulary design and patient access to medicines. Transparency into the findings of these formulary reviews are critical to understanding patient safeguards to access. Available at: https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/downloads/part-d-benefits-manual-chapter-6.pdf.

restrictions increased from 27 percent in 2010 to 47 percent in 2021.[220] This confirms previous research published by MedPAC that found Medicare beneficiaries now face access barriers for nearly half of all medicines covered in Part D.[221]

Further, changing incentives from the IRA could result in plans choosing to cover medicines very differently; they may impose tighter formularies or stricter utilization management than they have historically, jeopardizing beneficiary access, particularly for conditions where broad formulary access is critical. We note that therapeutically alternative medicines in a given class may not be appropriate for some patients who may need a particular medicine. For example, rheumatoid arthritis patients are more likely to fail on multiple medicines before having a positive clinical response to a given product. If plans narrow access to certain medicines due to dynamics introduced by government price setting, patients who are stable on a given medication may lose access and be forced to switch to an alternative medicines that is not optimal for their unique circumstances, which could result in adverse health outcomes.[222,223] With changing formulary dynamics caused by government price setting, PhRMA is concerned that formulary restrictions are likely to increase, resulting in significant risk to patients needing innovative medicines to treat difficult to treat conditions such as cancer and autoimmune conditions. Numerous studies have found that switching stable patients to a new medicine for non-clinical reasons leads to poor side effects and increased nonadherence and is often associated with negative health outcomes.[224] Given the potential for significant disruption as a result of the government price setting layered on top of Part D redesign, ***PhRMA recommends that CMS, through rulemaking, create safeguards that limit plan actions to disrupt patients who are stable on therapeutic regimens, including both selected drugs and their competitors.***

PhRMA urges CMS to maintain and protect the current Part D coverage standards for medicines. Part D requires plan formularies to include at least two drugs per class and all or substantially all of the drugs within the six protected classes of concern. We note that at least two drugs per class is a minimum standard which Part D plans can choose to exceed. Part D also requires plans to cover all or substantially all drugs in the six protected classes: immunosuppressants, antidepressants, antipsychotics, anticonvulsants, antiretrovirals, and antineoplastics. PhRMA has long maintained that these formulary protection standards are important to protect Medicare beneficiaries, many of whom have multiple chronic conditions with several medications that could contraindicate each other and who need access to a wider variety of medication options. According to a 2022 analysis by the CBO, per enrollee use of prescription medicines increased in Medicare Part D from an average of 48 prescriptions per year in 2009 to 54 in 2018,[225] a trend that will likely continue. Even without the substantial changes to the Part D program that are going to occur, in many cases, the vulnerable populations covered in Medicare and their health care providers need to have access to a broad range of medications, beyond just two drugs per class.

PhRMA recommends that CMS continue to enforce existing formulary requirements and important non-discrimination controls that ensure patient access to medicines. In the rapidly changing post-IRA environment, it is critical that CMS maintain and strengthen existing Part D beneficiary protections to ensure robust access to medicines. To protect patient access to affordable prescription medicines in Medicare Part D, CMS will need to

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[220] Marsh, T. (2021). The Big Pinch: New Findings on Changing Insurance Coverage of Prescription Drugs. GoodRxHealth. Available at: https://www.medpac.gov/document/july-2022-data-book-health-care-spending-and-the-medicare-program/.

[221] MedPAC. (2022). July 2022 Data Book: Health Care Spending and the Medicare Program. Data Book Chart 10-15, p. 27-28. Available at: https://www.medpac.gov/document/july-2022-data-book-health-care-spending-and-the-medicare-program/.

[222] American College of Rheumatology. (2023). American College of Rheumatology Position Statement: Patient Access to Biologics. Available at: https://www.rheumatology.org/Portals/0/Files/Patient%20Access%20to%20Biologics%20aka%20Model%20Biologics.pdf .

[223] Atzeni, Fabiola et al. (2016). Switching rheumatoid arthritis treatments: an update. Autoimmunity reviews. 10,7: 397-403. DOI:10.1016/j.autrev.2011.01.001.

[224] Nguyen E, Weeda E, Sobieraj D, et al. (2016). Impact of Non-Medical Switching on Clinical and Economic Outcomes, Resource Utilization and Medication-Taking Behavior: A Systematic Literature Review. Current Medical Research and Opinion. 32(7):1281-1290. Available at: https://pubmed.ncbi.nlm.nih.gov/27033747/.

[225] CBO Report. (2022). Prescription Drugs: Spending, Use, and Prices. Available at: https://www.cbo.gov/publication/57772#:~:text=Use%20of%20prescription%20drugs%20among,year%E2%80%94a%2013%20percent%20increase.

aggressively oversee Part D plan behavior when it comes to bidding, most notably around benefit designs that attempt to manipulate the Part D patient protections to hide discriminatory practices.

Further, CMS must not lose sight of the importance of strong beneficiary protections and appeals in the midst of so many fundamental changes to Part D. To that end ***PhRMA encourages CMS to re-examine and update rules around coverage determinations, appeals, and tiering exceptions*** to allow beneficiaries to appeal for lower cost sharing or exceptions for clinical reasons, to require clear language in Part D plan materials/websites that explains the exceptions process, and to allow medicines on the specialty tier to be subject to the tiering exceptions process. We also call on the Agency to enhance transparency and public reporting of these beneficiary protections and appeals outcomes.

Finally, in addition to rigorously maintaining and overseeing the existing Part D beneficiary protections, CMS should take additional steps to ensure meaningful choice of plans for beneficiaries. PhRMA is concerned that as the government drug "negotiation" program continues its annual process of selecting and setting prices for an increasing number of drugs, these dynamics could result in the rapid standardization of Part D plan formulary designs. Plans will be required to include all selected drugs on formularies and, in time, could also respond with severe access limitations on all competing non-selected drugs. This could lead to fewer meaningfully different options for beneficiaries to choose from when evaluating and selecting a Part D plan that will provide affordable access to their medications. It is imperative that CMS guard against these potential unintended consequences.

VIII. Conclusion

PhRMA appreciates your consideration of these comments. Please feel free to contact Jenny Bryant at jbryant@phrma.org or James Stansel at jstansel@phrma.org if there is any further information we can provide or if you have any questions about our comments.

-----s-------
Jenny Bryant
Executive Vice President
Policy, Research, and Membership
PhRMA

-----s-------
James C. Stansel
Executive Vice President and General Counsel
PhRMA

Exhibit A – Minimum Part D Data Fields Required for Verification of MFP-eligible Patients

In order to verify patient eligibility for the MFP and the calculation of MFP discount amounts owed by the manufacturer, at a minimum, CMS should ensure that manufacturers have access to the following minimum data fields on a detailed claims-level basis. Furthermore, CMS should also ensure manufacturers choosing to sell to pharmacies at a net price no higher than the MFP also have access to these data fields to improve program integrity. The majority of these data fields are already available through the PDE record, reducing the burden of sharing these fields with manufacturers.

Data Item	PDE Field Name (if Applicable)
Date of Service (i.e. date filled)*	Date of Service
Prescription ID Number*	Prescription Service Reference Number
Part D Contract ID and Part D Plan Benefit Package ID	Plan Contract ID and Plan Benefit Package ID
De-identified Part D Beneficiary ID	Medicare Beneficiary Identifier
Prescriber National Provider Identifier (NPI)	Prescriber ID
Pharmacy NPI*	Service Provider ID
National Drug Code (NDC)*	Product Service ID
Days Supply*	Days Supply
Quantity Dispensed*	Quantity Dispensed
Fill Number*	Fill Number
Paid Date (date the Part D plan paid the pharmacy)	Paid Date
Claim Status (whether the claim was paid or reversed)	
340B and non-340B Indicators (if adopted by CMS)	
340B Clearinghouse Determination (if adopted by CMS)	
340B Ceiling Price (received from Clearinghouse)	
Maximum Fair Price (MFP)	
Pharmacy Acquisition Cost**	
MFP Discount (Acquisition Cost less the MFP)**	

* These fields are already provided to manufacturers as part of the detailed data reports under the CGDP.

** This should be read consistent with PhRMA's position outlined in section I(f) of this comment letter that CMS should use an alternative metric such as WAC instead of acquisition cost.

Exhibit B – Example of Non-Disclosure Agreement

Attachment 5 Non-Disclosure Agreement

CONTRACTOR EMPLOYEE COMMITMENT TO PROTECT NON-PUBLIC INFORMATION NON-DISCLOSURE AGREEMENT FOR HEALTH AND HUMAN SERVICES/ASPR

I, _____ hereby consent to the terms in this Agreement in consideration of my being granted confidential access to certain United States Government documents or materials containing sensitive but unclassified information.

Access to non-public information may be required in the performance of my official duties, while working under the following contract or sub-contract with the Department of Health and Human Services (HHS), Assistant Secretary for Preparedness and Response (ASPR):

Contract Number _____ between _____ and my

employer _____.

To carry out the duties and functions of the United States (U.S), certain information may be disclosed to Contractors that are authorized representatives of the U.S. for the purposes of the disclosure and this Contractor Non-Disclosure Agreement. Such disclosure shall be considered authorized and not a disclosure to the public or outside the Government.

Should I have access to non-public information, I agree that I shall not release, divulge, publish, or disclose such information to unauthorized persons. I shall protect such information and will employ all reasonable efforts to maintain the confidentiality of such information. These efforts shall be no less than the degree of care employed by HHS to preserve and safeguard sensitive information. I will not disclose proprietary information designated "For Official Government Use Only" which has been received in connection with the Health and Human Services Professional Scientific Services contract, except on a need-to-know basis as instructed by the client. Prior to any disclosure to any other Government personnel or any other support contractor personnel, I will verify with the Contracting Officer/Contracting Officer Representative that the individual has signed a non-disclosure agreement with the Contracting Officer/Contracting Officer Representative substantially the same as this agreement. I understand that my obligation not to disclose information applies to information, which I have already received and to information I will receive in the future.

I acknowledge that the unauthorized disclosure of non-public information would violate this agreement; may additionally violate federal law, regulations or policy; and could form the basis for legal action against me or against my employer. I further acknowledge that unauthorized disclosure of said information may compromise the security of the HHS and violate the terms of the aforementioned contract with the United States Government.

I further certify that there are laws and regulations which provide for criminal and/or civil penalties for improper disclosure, including but not limited to:

18 U.S.C; 641 (Public Money, Property or Records)
18 U.S.C. 1832 (Trade Secrets)
18 U.S.C. 1905 (Disclosure of Confidential Information)
5 U.S.C.552a (Privacy Act)

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May 22, 2023

VIA ELECTRONIC FILING - REGULATIONS.GOV

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
Centers for Medicare & Medicaid Services
Department of Health and Human Services
7500 Security Boulevard
Baltimore, MD 21244-8016
Attention: PO Box 8016

Re: Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB, 0938-NEW)

Dear Deputy Administrator Seshamani:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit these comments in response to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act* (ICR or the ICR), including the Federal Register Notice, Supporting Statement – Part A, and ICR Form (CMS-10847, OMB, 0938-NEW).[1] PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA member companies have invested more than $1.1 trillion in the search for new treatments and cures, including $102.3 billion in 2021 alone.

PhRMA's comments on the ICR focus on: (1) the scope, necessity, and utility of the proposed information request for proper performance of CMS' functions relating to the Drug Price Negotiation Program (the Program); (2) ways to enhance the quality, utility, and clarity of the information to be collected; and (3) the burden estimate. PhRMA is particularly concerned with the vast scope of information requested, the unnecessarily burdensome approach CMS has proposed in how it defines certain types of data, and the inadequate time for manufacturers to prepare responses to such requests. Some of the data sought by CMS in the ICR extends beyond what is needed for the Agency to implement the Program, and conflicts with the Paperwork Reduction Act's requirement to collect information in the "least burdensome" way possible.

[1] 88 Fed. Reg. 16,983. (March 21, 2023). Centers for Medicare and Medicaid Services (CMS), Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act, Supporting Statement – Part A. Available at: https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847; CMS. (March 21, 2023). Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act, ICR Form. Available at: https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847.

PhRMA urges CMS to limit the data that must be provided within the thirty-day response period to elements that are essential to the operation of the Program, as outlined in these comments; permit manufacturers to respond with references to publicly existing data sources, where appropriate; limit submission of information that is already accessible to CMS; and allow additional time for submissions of supplemental data required by CMS for the MFP decision-making process after the October 2 deadline.

In addition, the lack of clarity of some of the terms used in the draft ICR, and the lack of flexibility CMS provides in response fields, will hinder submission of relevant, timely data by manufacturers and external stakeholders. Below we recommend specific changes to address this concern.

PhRMA has expressed concerns related to negotiation factors and data elements in comments filed in response to the *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for the Initial Price Applicability Year 2026, and Solicitation of Comments* (Guidance, or the Guidance). While we will reference some of our stated policy positions in this letter, we will not reiterate the full breadth of those comments here. As such, we encourage CMS to consider these materials in tandem for the full scope of our concerns and have thus attached our previous comments to this submission as Appendix A.

As noted in our comments on the Guidance, we are concerned generally with the lack of transparency, openness, and opportunities for manufacturer and stakeholder engagement in the maximum fair price (MFP) process that CMS proposes. A single ICR will not provide for adequate input and dialogue in this process, and the ICR mechanism is not well-suited for soliciting the wide range of data and research elements CMS will need in MFP decision-making, particularly in light of the novel and complex types of data and evidence required, and the importance of ensuring adequate weight is given to factors related to comparative clinical effectiveness and unmet medical need, which require consideration of a wide range of outcomes, evidence sources, and stakeholder perspectives. We urge the Agency to consider additional, complementary mechanisms to seek input, engage key stakeholders, and make publicly available the non-proprietary information it receives during the MFP process.

As previously noted in our comments to the Agency we also have concerns that the Data Elements ICR suggests an intent on the part of the Agency to over-rely on factors related to manufacturer costs and the flawed concept of "recoupment" of R&D and potentially drive to a "cost-plus" approach to price-setting. For example, the disproportionate number of fields requiring manufacturer-specific data, as well as the excessive and detailed data requirements proposed by CMS for manufacturer-specific data, indicate a potential for CMS to set MFPs based on "cost-plus" calculations. CMS' approach to determining MFPs for selected drugs has significant implications for patient access and biopharmaceutical innovation, and it is critical that the Data Elements ICR is aligned with an approach to price setting that focuses on the clinical benefit that selected drugs offer to patients, caregivers and society. As noted in our prior comments on the initial Guidance issued by CMS on the Program, we urge CMS to address this by making suggested changes to the ICR as detailed in the following comments by scaling back excessive and unworkable demands for manufacturer-specific data and strengthening the ICR's section on comparative clinical effectiveness and unmet medical needs.

I. Requirements of the Paperwork Reduction Act (PRA)

The PRA was enacted in response to the "enormous growth of our federal bureaucracy" and "its seemingly insatiable appetite for data."[2] Regulations implementing the PRA of 1995 establish that in order to receive Office of Management and Budget (OMB) approval, agency collection of information requests must demonstrate that the agency has taken "every reasonable step to ensure that the proposed collection of information:

[2] *United States v. Ionia Mgmt. S.A.*, 498 F. Supp. 2d 477, 487 (D. Conn. 2007), *citing Dole v. United Steelworkers of America,* 494 U.S. 26, 32 (1990).

(i) Is the least burdensome necessary for the proper performance of the agency's functions to comply with legal requirements and achieve program objectives;

(ii) Is not duplicative of information otherwise accessible to the agency; and

(iii) Has practical utility. The agency shall also seek to minimize the cost to itself of collecting, processing, and using the information, but shall not do so by means of shifting disproportionate costs or burdens onto the public."[3]

The Inflation Reduction Act (IRA) requires CMS to consider certain factors – five specific elements for manufacturer-specific information and evidence about alternative treatments – as the basis for determining offers and counteroffers for a selected drug under the Program. The IRA also contemplates submission of non-Federal average manufacturer price (non-FAMP) data for a selected drug.

As noted above, CMS' proposed requirements for data submission – particularly related to manufacturer-specific data – are well in excess of what the Agency needs to implement the IRA's MFP provisions and fall well short of the PRA requirements.

II. Concerns with How the ICR Aligns with Requirements of the PRA

As a starting point, the data requested is not the "least burdensome necessary" for CMS to perform its functions in compliance with the IRA and achieve program objectives, as required by the regulations implementing the PRA of 1995.[4] While CMS must collect certain data under the IRA, CMS proposes to collect such data in an unduly burdensome manner that goes well beyond the requirements of the IRA by requesting an extensive array of proprietary and non-proprietary data as well as expanding and subdividing data categories laid out in the IRA. The information CMS requests is both vast in its scope and imprecise, such that it raises serious burden and compliance concerns for manufacturers. Many of the elements will be impossible for manufacturers to collect such as in cases where the original developer of a product no longer exists. Other elements will be impossible for manufacturers to complete with the level of precision outlined in the draft ICR given current business practices for recording and accessing information.

The enormous breadth and detail of the information request, the challenges with quantifying some of the data elements with any degree of certainty, and the departure of requested data from current business practices, will create an exceptionally high burden and make compliance exceptionally challenging if not impossible within the thirty days permitted for response, affecting the ultimate utility of the data in contravention of the PRA. Further, the lack of clarity on many fundamental issues related to submission of data on treatment alternatives will further undermine the practical utility of the requested data. PhRMA is also concerned with the burden created by the short deadline for manufacturers to submit the data required by the ICR (at most, 31 days between date of selection on September 1, 2023 and date of submission on October 2, 2023). As noted in our Guidance comments, PhRMA believes CMS has the ability under the IRA to permit data submission from both manufacturers and other stakeholders beyond October 2, 2023.[5]

The data requested, in many areas, duplicates information already accessible to CMS through other means, in contravention of the PRA statute[6] and regulations, creating additional unnecessary burden on manufacturers.[7] CMS can alleviate burden induced by the tight timeline by allowing manufacturers to authorize CMS to access information readily available through other sources.

[3] 5 C.F.R. § 1320.5(d)(1)(i)-(iii).
[4] 5 C.F.R. § 1320.5(d)(1)(i).
[5] Guidance comments at I.c.
[6] 44 U.S.C. § 3506(c)(3).
[7] 5 C.F.R. § 1320.5(d)(1)(ii).

PhRMA views the highly burdensome requests of the ICR as unnecessary and without practical utility for CMS to comply with the requirements of the IRA or operate the Program. We urge CMS to carefully reconsider the data elements requested and limit them to those that are essential to the Program operations and leverage information in a form in which it is already available and accessible to the Agency. In addition, the Agency should consider complementary mechanisms, like stakeholder meetings or solicitation of comments, which could be used to gather input in a more effective, efficient manner.

III. General Comments and Recommendations

CMS is only in its first year of implementation of the Program that Agency officials have acknowledged is "novel" and "complex"[8] with an extraordinarily short period for implementation.[9] Moreover, CMS' simultaneous issuance of the Guidance and the Data Elements ICR means that the ICR incorporates definitions and concepts (such as the Primary/Secondary Manufacturer construct) that CMS presented as proposals that could change in final guidance in response to comment. This makes commenting on the ICR that much more difficult for stakeholders, who in their ICR comments cannot be certain of CMS' final policies. Rather than unnecessarily complicating its first-year collection of information, we urge CMS to seek information in the most flexible manner possible and allow manufacturers to present information under the plain terms of the statute.

CMS should thus provide a format for data collection that facilitates flexibility, consistency, and compliance rather than unjustifiably exposing respondents to potential liability. To this end, there are several areas where PhRMA has suggested that CMS not take an overly aggressive interpretation of very vague statutory terms and require excess detail and granularity of data that will be of low utility to the Agency.

Our recommendations are described in more detail below.

Follow Least Burdensome Necessary Approach:

In compliance with the PRA, CMS should reduce the data elements proposed for collection to those essential to operation of the Program. For data that are essential, CMS should ensure that the reporting is consistent with the ways in which data are typically tracked and recorded by companies or reported to the government. PhRMA provides specific recommendations below to this effect. Please see Section II.b. of PhRMA's Guidance comments for additional suggestions for CMS to be consistent with how data is collected and reported.

CMS could further alleviate unnecessary burden by abandoning the ICR's demand for use of detailed methodologies that do not comport with how data are currently available to manufacturers, as well as by allowing manufacturers to authorize CMS to access information readily available through other sources.

CMS could also alleviate burden by requesting only one year of data be provided for some financial data elements such as various market data, revenue, and sales volume data. Please see our comments below in Section IV on "Market and Revenue Data" regarding the recommendation to collect less than 5 years of data.

Avoid Duplication of Information Available to the Agency:

Some of the data CMS is requesting is already accessible to the Agency from other sources. To avoid unnecessary duplication, CMS should permit manufacturers to provide references to publicly available sources (*e.g.*, the Food and Drug Administration's Drugs@FDA database, the Orange Book, and the Purple Book) or provide a box to check affirming that CMS may use other (including non-public) sources

[8] 87 Fed. Reg. 62433 (October 14, 2022)
[9] Castronuovo, C. (2023). Drug Price Negotiations Need 'Nimble' Approach, Official Says. Bloomberg Law. Available at: https://news.bloomberglaw.com/health-law-and-business/drug-price-negotiations-need-nimble-approach-official-says

of information in lieu of duplicating this information via the submission. We believe CMS has erroneously concluded that manufacturers must provide a full re-submission of already available data, even if the manufacturer were to agree that CMS' use of a specific source of data (including cases where CMS can obtain non-public data available to the Agency) constitutes the manufacturer's "submission" of such data.[10] Consistent with the PRA, however, CMS should provide greater flexibility, and find that a manufacturer agreeing that CMS may obtain data from an already-available source, or citing to a publicly available reference, is tantamount to an affirmative submission.

Ensure Practical Utility of Submission Requirements:

To ensure practical utility of the data for CMS, companies should be able to explain the data elements in a more unstructured way, as long as reasonable assumptions are documented and disclosed to the Agency. A less structured, more flexible approach, especially in the first few years of the program, will enable CMS to gain greater knowledge and better use of data points. This includes eliminating text limits and providing more flexibility for the submission of data CMS is seeking, for example on the evidence about alternative treatments, which is likely to be voluminous given the years on the market at time of selection. In its current approach CMS is shortchanging its ability to best understand the medicines selected for their Program by confining submission to a limited number of words and rigid data fields with very little utility, given the price-setting methodology outlined in the guidance. Eliminating character and word limits gives manufacturers the ability to better explain their data elements and therefore provides CMS a better understanding of what data has been submitted.

In addition, some manufacturer data will be most useful to the Agency, as well as less burdensome, if the fields are rolled up into a single question and single global response with an unlimited narrative field, such as for the fields dedicated to capturing the costs of research and development (R&D) for the selected drug. Eliminating character and word limits gives manufacturers the ability to better explain their data elements and therefore provides CMS a better understanding of what data have been submitted. As highlighted in our guidance comments and discussed further below, PhRMA does not believe that CMS should be capturing R&D cost data at a granular level and should instead amend the ICR to allow a single global response for R&D costs, similar to a Form 10-K for Securities and Exchange Commission (SEC) filing, and a single attestation (YES/NO) regarding the extent to which these costs have been "recouped." As noted in our guidance comments, we believe the standard of R&D "recoupment" is fundamentally misguided, unworkable, and difficult if not impossible to quantify with any degree of precision. Therefore, if a manufacturer of a selected drug estimates that R&D costs have not been "recouped," or even if they estimate costs have been "recouped", they should be able to provide more explanation of this to CMS, including narrative on manufacturer's level of certainty and thoughts on the "extent to which" costs have ben recouped. In our detailed comments we outline a flexible approach the Agency could allow for manufacturers to explain their selection.

Related to the practical utility concerns discussed above, it is critical that CMS establish submission requirements that are workable based on the reality of corporate and legal structures in the industry. As PhRMA explained in detail in our Guidance comments, "Primary Manufacturers" may not have a right to access "Secondary Manufacturer" information and thus, the proposed Primary/Secondary Manufacturer policy contemplated in the Guidance and in this ICR should not and cannot be adopted. We are concerned that this ICR contains unreasonable assumptions related to a Primary Manufacturer's ability to access data requested from Secondary Manufacturers. Furthermore, given that this information is highly sensitive, if third parties share information about contracts they have with an impacted manufacturer, the manufacturer should be notified in order to have the ability to confirm or clarify the provided information.

[10] We believe CMS' erroneous conclusion is based upon statutory language stating that the Secretary should consider certain data with respect to the selected drug "as submitted by the manufacturer." SSA § 1194(e)(1).

CMS could improve the usefulness of the information it receives (and facilitate manufacturer compliance with data submission requirements) by exercising its discretion to permit submission of data after the October 2 deadline. In the ICR, CMS appears to recognize discretion to solicit information outside of specific statutory deadlines,[11] and we strongly encourage the Agency to recognize this discretion as it applies to manufacturer-specific data as well and provide explicit, complementary opportunities to submit information.

Provide Transparency for Manufacturers of Selected Drugs:

CMS could still improve the process by sharing with the selected drug manufacturer nonproprietary evidence submitted on alternative treatments by third parties. Individuals or entities submitting information should be required to indicate whether evidence submitted is proprietary or non-proprietary. Any non-proprietary data, particularly data submitted under Section 1194(e)(2) or data that specifically identifies a manufacturer should be shared with the selected drug manufacturer. Relatedly – and in addition to our broader comments on the Guidance on the importance of CMS making publicly available the non-proprietary data it receives under 1194(e)(2) – the system should provide an upload function for respondents submitting evidence about alternative treatments to upload information, studies, and related documents and in doing so, automatically share such studies with the selected drug manufacturer.

Protect Confidentiality of Proprietary Data:

CMS acknowledges that much of the information to be submitted by selected drug manufacturers will constitute proprietary information and that such information "shall only be used by CMS or disclosed to and used by the Comptroller General of the United States for purposes of negotiation."[12] To facilitate the identification of proprietary information, CMS should allow for checkboxes or other means for manufacturers to easily designate submitted information as proprietary. In addition, CMS should develop and solicit comments on a robust confidentiality and data security protocol for protecting manufacturer proprietary information. Please see Section I.d. of PhRMA's Guidance comments for additional recommendations and comments on CMS protecting proprietary information.

Do Not Penalize Responses Provided in Good Faith

The IRA may impose substantial Civil Monetary Penalties (CMPs)[13] and excise taxes[14] when a manufacturer does not submit certain information or submits "false information." In light of the types of challenges described above related to manufacturer submission of data from a wide range of sources, some of which will be very difficult to calculate, as well as the need to rely on reasonable assumptions, CMS should publicly affirm that when manufacturers respond in good faith, with reasonable assumptions identified, they are not subject to these penalties. As discussed in more detail throughout these comments, the ICR could exacerbate the risk of potential liability by requiring manufacturers to submit vast amounts of data in a format that does not accord with typical business practices, including by requiring Primary Manufacturers to obtain data from Secondary Manufacturers that they may not have access to, through unclear definitions, and by requiring completeness and accuracy but then imposing arbitrary word limits. Manufacturers may need to reconfigure financial systems, develop assumptions that are inconsistent with other federal programs (e.g., SEC , and break down data in a new and highly prescriptive way to delineate data in the manner CMS requests, and for the sole purpose of the price-setting process. CMS should therefore create safe harbor-like standards that afford manufacturers prospective assurances that they can, using best efforts and in good faith, submit the novel information

[11] See Supporting statement at 2, stating: "This ICR Form serves as one of multiple ways that CMS intends to collect data per Section 1194(e)(2)."
[12] Supporting statement at p.6.
[13] SSA § 1197(b) and (c).
[14] IRC 5000D(b)(4).

CMS is requesting without the threat of extreme penalties. We also refer CMS to, and incorporate here, PhRMA's extensive discussion on these issues in Section VI of our Guidance comments.

IV. Manufacturer Data

This section of our comments delineates examples of PhRMA's areas of concern based on the vastness of information requested. These comments endeavor to ensure that the data required are essential to the operation of the Program and align with the PRA.

Non-FAMP Data Collection

CMS requests that manufacturers submit the non-FAMP for selected drugs, following specifications set forth in the ICR. For IPAY 2026, manufacturers are instructed to complete a table about the non-FAMP, using the reported National Drug Code (NDC)-11s and quarterly non-FAMP and total package unit volume to compute the average non-FAMP for calendar year 2021.

As set forth in our Guidance comments, PhRMA recommends that CMS use the annual non-FAMP already reported by manufacturers to the U.S. Department of Veterans Affairs (VA) as defined in 38 U.S.C. § 8126(h)(5). For 2021, this data would be the annual non-FAMP value reported to the VA by November 15, 2021. Such use of already available sources would accord with the PRA, which prohibits "any federal agency from adopting regulations which impose paperwork requirements on the public unless the information is not available to the Agency from another source within the Federal Government,"[15] and which requires each agency to "manage information resources to…reduce information collection burdens on the public."[16] PhRMA also recommends that manufacturers have the ability to make timely restatements to CMS in the event that the manufacturer restates non-FAMP values.

PhRMA further requests that CMS clarify that the units for non-FAMP may be different than the units on the Part D Prescription Drug Event (PDE) record, which uses National Council for Prescription Drug Program (NCPDP) defined values. CMS should recommend that manufacturers report the unit measure for non-FAMP in the explanatory field for Section B. More specifically, for all pricing metrics, the unit the manufacturer reports should match the unit used in the original metric. CMS should not transfer the burden nor rely on manufacturers to accurately crosswalk reporting of unit values between the two standards in Definitions for Section G, for unit type and unit of measure (CMS Medicaid units and the NCPDP billing unit standard). Due to the burden on respondents, as well as the CMP implications and related exposure, CMS must perform any cross-walking necessary. We request that CMS refer to our detailed comments on the Guidance related to non-FAMP in evaluating the ICR Data Elements.

As CMS recognizes in its supporting statement, "non-FAMP data is proprietary information"[17] and, as such, a Primary Manufacturer does not have access to Secondary Manufacturer non-FAMP data. As noted in our Guidance comments, CMS previously concluded that including sales of a Secondary Manufacturer within a Primary Manufacturer's AMP calculation "would be problematic from an administrative accounting and anti-trust perspective."[18]

R&D Costs and Recoupment

The IRA provides for manufacturer submission of R&D costs of the manufacturer for the drug and the extent to which the manufacturer has recouped those costs. We urge CMS to refer to Section II.b. of PhRMA comments where we raise concerns around the general validity of CMS's approach to capturing "R&D recoupment," and to modify the ICR to recognize both the inherent problems with the concept and

[15] *Dole v. United Steelworkers of America,* 494 U.S. 26, 32-33 (1990).
[16] 44 U.S.C. § 3506(b)(1)(A).
[17] Supporting statement at p.6.
[18] PhRMA Initial Guidance Comment Letter at 14; 72 Fed. Reg. at 39200 (Jul. 17, 2007).

the challenges of quantifying it with any degree of certainty. The ICR requests a far broader and more detailed array of data than necessary, some of which appear grounded in erroneous assumptions about manufacturers' ability to gather such data, which significantly increases the difficulty and burden of complying with this requirement. Specifically, CMS seeks dollar amounts for R&D, as well as explanations of how costs were calculated, where applicable, related to six categories: (1) basic pre-clinical research for all approved indications of the selected drug; (2) post-IND costs for all approved indications of the selected drug; (3) costs of all completed, Food and Drug Administration (FDA)-required Phase IV studies for the selected drug; (4) costs of all post-marketing trials for the selected drug; (5) costs of failed or abandoned products related to the selected drug; and (6) costs of other R&D for the selected drug not accounted for in the preceding questions. Cost data and explanations are also requested related to global, total lifetime manufacturer net revenue for the selected drug, as a way to assess recoupment of R&D costs for a selected drug. CMS describes a breakdown of costs into what they believe to be mutually exclusive categories.

PhRMA is concerned about the breadth of the information requested, the specificity and novelty of CMS' six-part subdivision of R&D costs, the compressed period for gathering and submitting such atypical information, and the assumptions that the R&D costs can be broken down in the specific terms sought related to the labeled indications for a selected drug. This specificity is particularly challenging for manufacturers with regard to the costs of preclinical research. CMS' reporting methodology is not consistent with how manufacturers track cost information, thus raising concerns for companies seeking to comply under a very tight deadline, particularly in the first year of the program. CMS' reporting methodology is not clear as there could be overlap in how costs are allocated, for example allocation of indirect expenses could apply to multiple categories. Manufacturers also may not have documentation and retention policies that would allow them to reconstruct all the R&D costs of products that have been on the market for seven or eleven years, and which were under development for many years before approval, at the level of specificity that CMS is requesting. CMS' interpretation of forms of a drug extending to all active moieties and active ingredients only compounds this complexity. Practical concerns related to these proposals are set forth in detail in Section II.b. of our comments in response to the Guidance, and we incorporate those comments by reference here as well.

CMS uses disparate standards at different places in the ICR, potentially leading to miscalculations of R&D costs and recoupment. Specifically, the ICR limits calculation of R&D costs to "FDA-approved indications," but then seeks data on "global lifetime revenue." This incongruence will not only yield inaccurate estimates but is unduly burdensome with regard to how manufacturers actually track R&D expenditures. PhRMA previously raised the concern in our comments that companies do not consider drug development costs related to specific market applications only. In fact, companies regularly utilize global clinical trials to facilitate the goal of simultaneous market access in as many countries as feasible when considering their product development and launch strategies. In addition, the global lifetime revenue of a drug will necessarily include revenues from markets outside the U.S. Bifurcating the requests for development costs vs. recoupment revenues in a U.S. market-based approach for costs but a global approach for recoupment creates additional complexity and unnecessarily increases the compliance risks for manufacturers without providing a clear benefit for CMS' ability to determine the MFP offer.

The ICR, as drafted goes beyond the plain language of the IRA. The IRA states only that a manufacturer should submit information on: "research and development costs of the manufacturer for the drug and the extent to which the manufacturer has recouped research and development costs."[19] In accordance with this statutory direction, CMS should focus only on whether a company has recouped the cost of R&D. CMS' requested level of detail is unnecessary and the categories are not helpful for CMS to determine whether R&D has been "recouped" under 1194(e)(1). Not only does the submission of such data in granular categories create undue burden on manufacturers, but it is also unclear in the ICR why the R&D

[19] SSA § 1194(e)(1)(A).

data must be broken out in the format specified. Each company tracks and manages R&D spending differently, and CMS' rigid outline of costs does not account for such variability.

To address these inconsistencies and reduce manufacturer burden, PhRMA recommends that CMS amend the ICR to allow a single global response for all the manufacturer's R&D costs across all development programs, similar to a Form 10K for Securities and Exchange Commission (SEC) filing, and a single attestation (YES/NO) for recoupment. If a respondent stipulates "YES" that they have recouped research costs, then CMS need not gather any additional information. If a manufacturer checks "NO," then the manufacturer should be allowed the flexibility to provide an explanation, free of word limits, as to how the costs weren't recouped through one or more of the following approaches. These could include allowing manufacturers to allocate a percentage of total R&D to the selected drug based on a generally accepted standard (e.g., 20% of total R&D spending to the selected drug based on historical actual or budget) and a free text box to explain how that calculation was derived. Another approach, based on data availability, would allow manufacturers to provide data in two broader categories: (1) costs of R&D *before* initial FDA approval (an aggregate way to gather all basic/preclinical and clinical development), and (2) costs of R&D *after* FDA approval, which would include Phase IV costs, allowing for reasonable assumptions and allocations of spending for the selected drug. Other approaches provided by the manufacturer and including reasonable assumptions and methodologies should also be acceptable for CMS.

As the ICR stands currently, manufacturers are very likely to exceed the full 500 hours CMS projects for completion of the entire ICR on this section alone. PhRMA urges CMS to amend the ICR to the single global response and associated free text field for explanation as recommended above to ensure a workable and "least burdensome" approach.

Current Unit Costs of Production and Distribution

The ICR sets forth a methodology for calculating and reporting current unit costs of production and distribution for each NDC-9 included in the selected drug, as well as any NDC-9 of the drug marketed by a Secondary Manufacturer. PhRMA is concerned with the broad, overly burdensome request in a manner that extends beyond the terms of the IRA. In addition, the ICR contemplates manufacturer submission of data that may not be available to them, such as data residing with third-party suppliers and others in the supply chain. We incorporate our Guidance comments from Section II.c. for additional concerns on this Section.

CMS should revise the ICR to provide discretion to manufacturers to describe production and distribution costs that they are able to report and offer a narrative explanation, without word limits, for how the costs were computed and to flag other considerations that may impact production and distribution, rather than specifying a detailed methodology that may not mirror how these costs are recorded and tracked by different manufacturers. Breaking down current costs of production and distribution by drug is difficult and such data is not typically recorded at the NDC-9 level. Production costs are not typically allocated based on a per-product basis and, from an accounting perspective, are not tracked at the NDC level.

Prior Federal Financial Support

CMS requests prior Federal financial support for novel therapeutic discovery and development related to the selected drug. This includes support from when initial research began or when the drug was acquired by the manufacturer, until the date of the most recent NDA/BLA approval for the selected drug. CMS seeks financial support dollar amounts and supporting explanations related to tax credits (General, R&D); Orphan Drug Act and other specific tax credits; Direct Federal Financial Support of Development; NIH Grants; Department of Defense (DOD) Congressionally Directed Medical Research (CDMR) Funding; Defense Advanced Research Projects Agency (DARPA) Funding; and other federal financial support not

included elsewhere. CMS also seeks details on agreements between the manufacturer and the federal government, such as licensing or purchasing agreements.

PhRMA strongly recommends that consideration be limited to funding that resulted in a patent application containing a Government Interest Statement and/or research where a patent assignee was a U.S. government agency for an invention directly related to the development of the selected drug (*e.g.*, excluding basic science, research tools, or similar general concepts). To comply with the PRA, CMS should obtain this information through other, already-available sources, rather than procuring it entirely from manufacturers. In addition, the federal financial support chart should request only one field with the total federal financial support figure, along with an explanation. The burden and difficulty of obtaining data in the specific manner CMS requests in these fields significantly outweighs the utility of this data for the Program.

We are concerned that CMS strays far beyond the statute for this data element. Our recommendation, of one total figure directly related to the selected drug, is more in line with the statute. The IRA only requires one line-item for reporting prior support and states that the manufacturer should submit "prior Federal financial support for novel therapeutic discovery and development with respect to the drug."[20] Moreover, if CMS is to limit R&D manufacturer costs to FDA-approved indications for the selected drug, CMS similarly should be consistent and consider only the federal financial support directly relevant to such labeled indications. To that end, general tax credits that are not product-specific should not be considered.

Further, CMS should clarify that prior federal financial support that must be reported is only for the period starting from when the manufacturer acquired the drug, even if this methodology may result in reporting of no prior federal financial support during the period for products associated with patent applications that included a Government Interest Statement.

In relation to CMS' requests relating to agreements between the manufacturer and the federal government, such as licensing or purchasing agreements, manufacturers may not continue to have access to these documents, depending on document retention policies. Even if this information is available, divulging it may represent a breach of contract or confidentiality within parties.

Patents, Exclusivities, Applications, and Approvals:

The ICR requests data on "pending and approved patent applications," exclusivities recognized by the FDA, and applications and approvals pursuant to Section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) or Section 351(a) of the Public Health Services Act (PHSA).

PhRMA urges CMS to procure information on "approved patent applications" from the FDA's Orange Book and Purple Book listings and information about approved applications under the FDCA and PHSA from Drugs@FDA. Doing so will better align with the PRA's requirement for the Agency to refrain from seeking information that is duplicative of data already accessible to the Agency. As set forth in our preceding general recommendations, manufacturers should be permitted to check a box stating that CMS may use these publicly available resources in lieu of manufacturer submission of duplicative data. Companies should be permitted to similarly reference these sources, as needed, in responses rather than duplicating the information.

As stated in Section II.e. in our Initial Guidance comments, CMS should consider only those patents and patent applications that are directly related to the selected drug. CMS could further align with the PRA and clarify the currently vague definition of relevant patent information, which could encompass collection of information with little utility for the Program such as information on patents and patent applications that have no bearing on the continued single-source status of a selected drug. Rather, CMS

[20] SSA § 1194(e)(1)(C).

should focus as noted in Questions 13 and 14 on patents that claim the drug substance, drug product, or method of using the drug. CMS should accordingly delete the reference to manufacturing processes in the text of Question 14. Furthermore, CMS should amend the ICR to reflect the comments made in Section I.d. of our Initial Guidance comments, relating to the confidentiality of pending patent and FDA applications, which typically contain information that is proprietary, highly sensitive, and would also not have utility to CMS for the purposes of the program as they may be rejected or voluntarily withdrawn. In addition, as noted in our prior comments, CMS should confirm that "abandoned" patent applications do not constitute "pending and approved patent applications."

Market Data, Revenue, and Sales Volume Data

Under the category of market data, revenue, and sales volume data, CMS seeks to collect an extensive set of pricing data, including federal price reporting metrics and commercial prices, as well as acquisition costs, gross revenue, net revenue, net revenue without patient assistance programs, and quarterly total U.S. unit volume.

This section of the ICR represents a serious overreach by the Agency related to its authority to request information from manufacturers necessary for operation of the Program over such a significant period of time. The data elements required under this section must be reported for each quarterly period in the most recent five years, presenting a substantial burden without any basis in statute. Additionally, as discussed earlier in this letter, this section of the ICR raises significant concerns related to "primary manufacturers" reporting these data on behalf of "secondary manufacturers" as this could violate contractual agreements.

Furthermore, the only pricing metric that the IRA indicates manufacturers must report to CMS under the Program is non-FAMP. CMS cannot use the general term of "market data, revenue, and sales volume" to obtain broad propriety pricing information for a selected drug in nearly all market segments. These data points are not necessary or essential to the operation of the Program, their inclusion in the Program could create a disincentive for manufacturers to offer discretionary discounts to other federal programs and payers, and CMS provided no rationale for collecting such data, in either the Initial Guidance or in the ICR. Moreover, the ICR would require manufacturers of selected drugs to calculate and report various new and confusingly-described pricing metrics – which would require that manufacturers develop reasonable assumptions to use in calculating these metrics and report their reasonable assumptions – which assumptions may be difficult to describe correctly given the word limits on manufacturer responses.

In relation to questions 21 – 24 of the ICR (340B Ceiling Price and 340B Prime Vendor Program Price), CMS already has access to the 340B Ceiling Price through existing price reporting under the Medicaid program. However, the 340B Ceiling Price and 340B Prime Vendor Program price both have no bearing on Medicare "negotiation" and, as such, should not be included in the data requested. The IRA refers only to submission of non-FAMP, not other price reporting metrics, and requiring manufacturers to report sub-ceiling 340B pricing information could create a significant disincentive for manufacturers to continue to offer sub-ceiling discounts. Additionally, HHS already has access to the 340B utilization volume through the HRSA Prime Vendor data, although again the 340B utilization volume is not a required statutory data element and does not have bearing on IRA negotiation.

As for questions 25 – 30, which request Medicaid Best Price, Federal Supply Schedule (FSS) Price, and the Big Four Price, CMS already has access to Medicaid Best Price through existing price reporting to the Agency under the Medicaid program, and FSS prices are publicly reported. However, Best Price, FSS Price, and the Big Four Price are not appropriate reference points for Medicare and therefore lack utility. As noted in PhRMA's Guidance comments, the Senate overwhelmingly rejected (by 99-1) amendments

that would have incorporated FSS and "Big Four" pricing into the IRA,[21] and these price metrics already reflect negotiation by the federal government. Please refer to Sections II.f. and III.a. of PhRMA's prior comments for additional explanations as to why Veterans' Affairs pricing (which uses "national formularies . . . of preferred drugs, steer[s] patients to lower-cost drugs, and buy[s] drugs in large volumes"[22]) is not representative of "market" pricing and is not an appropriate model for setting Medicare prices. Similarly, Best Price is a Medicaid, not a Medicare, metric. Congress has historically allowed Medicaid, a program for the lowest income and most vulnerable U.S. populations, to act as payer of last resort and receive prices that are far lower than other pricing. And again, the IRA statute refers solely to submission of manufacturer non-FAMP, not to these pricing metrics.

In questions 31 – 34, CMS has created new methodologies (*i.e.*, multiple variations of "U.S. commercial average net unit price" and "manufacturer average net unit price to Part D plan sponsors") on which manufacturers need to report within the 30-day time period, including explanations as to how certain terms are treated and allocated, as well as how certain classes of trade were handled. First, commercial pricing data is not necessary or essential to the operation of the Program and should not be a required data element. The IRA statute refers only to submission of non-FAMP, not commercial pricing metrics, and furthermore, patient assistance is not a price available to either commercial payers or federal programs. Second, development and validation of these types of methodologies within 30-days is an unreasonable request and, again, places undue compliance burdens on manufacturers seeking to compliantly respond to the ICR. The new metrics are not defined with specificity and the lack of clear definitions will likely result in inconsistencies,[23] and the requirement for manufacturers to provide data on these new metrics covering quarterly periods for five years creates a particularly excessive burden. CMS should withdraw these new metrics, and the corresponding fields in the ICR, in their entirety. To the extent CMS is not willing to do so it should, at a minimum, define patient assistance and exempt manufacturer charitable free drug programs. For U.S. commercial average net unit price, CMS should explicitly exclude FSS and the Big Four Price from this metric, as they are not commercial prices. For U.S. commercial average net unit price, CMS should explicitly exclude all prices that are not prices to commercial customers from this metric. In addition to the excluded price and volume information already listed for Medicare and Medicaid, minimally FSS prices, the Big Four Price and 340B Ceiling Price should also be specifically excluded.

CMS should focus this section on data that are market data, revenue, and sales volume data, such as gross and net revenue and sales volume. There is no legitimate reason for CMS to request the pricing data as part of this ICR and we incorporate Guidance comments in Section II.e. of our letter that touch on this element of data collection as well.

V. Evidence About Alternative Treatments

Primary manufacturers and interested third parties may submit information on the factors described under Section 1194(e)(2) of the SSA on the selected drug and available therapeutic alternative(s) under the "Evidence About Alternative Therapies" section of the ICR.

Although all questions in this portion are voluntary for both manufacturers and public data submitters, CMS is required by statute under Section 1194(e)(2) to consider evidence about alternative treatments "as available." Many experts and stakeholders have noted the important role that this information will play in

[21] 24 S. Amdt. 5210 to S. Amdt. 5194 to H.R 5376. Available at: https://www.senate.gov/legislative/LIS/roll_call_votes/vote1172/vote_117_2_00288.htm.
[22] Congressional Budget Office. (2021). A Comparison of Brand-Name Drug Prices Among Selected Federal Programs. Available at: https://www.cbo.gov/publication/57007.
[23] CMS should be well aware that other mandatory pricing metrics (such as Average Manufacturer Price, Best Price, and Average Sales Price) have involved nuances in definition that have taken many years to fully address. Creating completely new mandatory pricing metrics under such short timelines for consideration risks an ill-defined and ill-targeted metric.

the MFP process.[24] Manufacturers will also need to consider 1194(e)(2) factors when responding to a CMS "initial offer" via a counteroffer. Thus, while technically voluntary under statute, it is important for the Agency to recognize that, as a practical matter, many manufacturers and other stakeholders (including, potentially, manufacturers of therapeutic alternatives that may also indirectly be evaluated in comparison to the MFP-selected drug) will feel compelled to submit evidence and data under this section. In light of the important role these factors can and will play in the MFP process, we believe CMS should provide additional detail and clarity to facilitate timely submission of relevant information on these factors. In addition, the breadth and complexity of this information, and its importance to patients, caregivers and public health, reinforce the importance of CMS establishing supplementary mechanisms for gaining ongoing stakeholder input (for example, for patients, caregivers and physicians). CMS will not be able to gain a complete and accurate picture of factors such as relative clinical benefit and unmet need without a) properly and clearly defining these terms and b) engaging patients, physicians and other stakeholders on an ongoing basis.

As currently requested in the ICR, CMS does not provide adequate clarity or time for respondents to provide the information necessary for CMS to properly conduct and synthesize patient-centered clinical effectiveness research and costs of selected drugs and treatment alternatives. Further, submission of these data by manufacturers and public stakeholders could be particularly challenging due to the large volume of research that will have accumulated for medicines as a result of post-approval research across multiple forms and indications. The arbitrary word counts and citation limits, particularly the 1,000-word limit on questions 40 and 43, are concerning given the complexity of the issues presented and the primacy CMS proposes to give net price of therapeutic alternatives in its price setting. As such CMS should remove these limits to allow for biopharmaceutical manufacturers and the public to submit all the data necessary for CMS to consider. Furthermore, as many members of the public, including patients and clinicians, may not be able to collect the volume of data requested, CMS should allow Section H to be submitted throughout the price-setting process. As the time constraint will prove a challenge for manufacturers, it will be even more so for representatives from underserved or underprivileged communities that may not have the resources to compile these data together within the provided window. Our concerns regarding substantive and technical components of this section are set forth below.

Minimize Burden on Respondents

As currently proposed, respondents are asked to submit all information on all potential comparators across all indications within the 30-day deadline, with no bounds on the potential universe of products. PhRMA is very concerned about the open-ended nature of this question and the practical utility to CMS of such an open and undefined data set. If selected therapeutics alternative(s) are not identified in advance, more manufacturers of *potential* therapeutic alternatives likely will feel compelled to submit data on these factors, thereby increasing unnecessary burden of data submission for stakeholders. To minimize burden of submission and increase likelihood that the information submitted to CMS is relevant and useful, CMS should publicly identify the therapeutic alternative(s) as well as any resources (e.g., manufacturer feedback, clinical guidelines, advisory panels, etc.) it relied upon to identify the therapeutic alternative(s) when the drugs selected for negotiation are announced. As noted in Section III.c. of our Guidance comments, experts, including manufacturers and clinicians, should be the primary resources for determining therapeutic alternative(s).

Avoid Duplication of Information Available to CMS

Under Question 40, CMS requests prescribing information to which the Agency already has access; it is unnecessarily burdensome to collect these data again through this ICR. In particular, the first bullet under the subheading, "Question to Respond to for Question 40," requests information on prescribing

[24] Bright, J., Oehrlein, E. M., Vandigo, J., Perfetto, E. M. (2023). Patient Engagement Data: Missing Ingredients for CMS' Successful IRA Implementation. Health Affairs Forefront. Available at:

information that has been approved by the FDA for the selected drug and therapeutic alternative. This information is accessible already and is redundant to FDA prescribing information available from Drugs@FDA. CMS should remove this bullet or clarify that this information is already publicly available FDA prescribing information and will be procured by CMS.

Clarification of Evidence Standards

CMS is not permitted to rely on quality-adjusted life-years (QALYs) or similar measures as part of the MFP process, as noted by CMS in the initial Guidance on the Program. However, PhRMA is concerned that the manner in which CMS instructions submitters to limit submission of comparative effectiveness research that relies on QALYs or similar metrics in the instructions for Questions 40-41. CMS instructs the submitter against submission of "evidence comparative clinical effectiveness research that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill", a reference to the prohibition on reliance on QALYs and similar metrics found in the statute. This instruction ignores the fact that CMS is also prohibited from reliance on QALYs, and similar metrics of cost effectiveness analysis under Section 1182 of the SSA, which does not include that qualifier. Whether or not research treats extension of life benefits differently for certain population is not the only applicable standard, and CMS should revise its language accordingly.

Furthermore, this prompt is not an attestation and will not provide any additional information that will inform CMS' use of the data, as CMS should evaluate all data submissions to protect against use of the QALY or other discriminatory metrics, and therefore should be deleted. As noted in Section II.g. of our Guidance comments, CMS fails to sufficiently define "clearly separated" to allow stakeholders to understand what information is prohibited and considered discriminatory by CMS. CMS does not have the time and expertise to review the large quantities of data to be submitted through the ICR to separate out the information in the study that is relevant to the price-setting factors but does not implicate the use of QALYs or other discriminatory metrics. Instead of spending time judging if the information submitted to CMS meets this vague and unnecessary standard, CMS should require all data submissions to remove all QALY-based information. Furthermore, CMS should thoroughly review all evidence submitted through this section of the ICR to ensure that the MFP determination does not rely on the QALY or other metrics that treat the lives of vulnerable populations – including the elderly, disabled, or terminally ill – as of lesser or lower value.

To help ensure CMS receives appropriate data, PhRMA also urges CMS to provide general clarification on the evidence standards for submitted data (*e.g.*, guidance on whether studies must be U.S.-based, types of studies accepted, rigor, evidence hierarchy, etc.). While biopharmaceutical manufacturers should have the ability, without word or citation limits, to provide a wide range of evidence that they can justify as accurate and appropriate for CMS to consider in MFP decision-making, it is critical that CMS help reduce the burden on data submitters by helping them to tailor their submissions to prioritize evidence that meets Agency standards. Further, CMS should outline whether there are levels of evidence that must be met for data provided from external stakeholders. This is especially important for the collection of real-world evidence as it can come from many sources and vary widely in quality, so CMS must specify guardrails to ensure submission and evaluation of high-quality and rigorous evidence. These guardrails should exist to ensure that public data submitters follow similar standards (e.g., pre-specified protocols, transparency, and use of fit-for-purpose data). Examples of these guidelines can be found from established professional societies such as ISPE (International Society for Pharmacoepidemiology)[25] and ISPOR (The Professional

[25] Sobel, R. E., Girman, C. Ehrenstein, V., Nyberg, F., Soriano-Gabarró, M., Toh, D. (2020). ISPE's Position on Real-World Evidence (RWE). International Society for Pharmacoepidemiology. Available at: https://pharmacoepi.org/pub/?id=136DECF1-C559-BA4F-92C4-CF6E3ED16BB6

Society for Health Economics and Outcomes Research).[26]

Clarification of Terms

PhRMA requests clarification and definition of key themes and terminology included in the ICR. As the ICR is open to the public with various levels of pre-existing knowledge regarding CMS' price-setting process, PhRMA recommends that CMS provide definitions of the key terms used in Section H at the beginning of each question and in the instructions to help stakeholders understand what information CMS is seeking. Examples of areas of concern are set forth below:

- Personal Experience: CMS should change the terminology of "personal experience" under the subheading, "Instructions for Questions 40 through 43," to expand beyond that of taking or prescribing the medicine described in the outlined narrative. The Agency should also include and collect important voices from any interested patient, clinician, caregiver, or patient advocate. Thus, CMS should carefully word these definitions to be inclusive and explicitly encourage these individuals to submit information. As noted in the Patient-Centered Outcomes Research Institute's Equity and Inclusion Guiding Engagement Principles: "inclusion of diverse perspectives and groups in research partnerships goes beyond achieving categorical representation; it requires explicit invitations, clearly stated intentions, culturally appropriate actions, humility, and the deliberate creation of welcoming environments that foster a sense of belonging."[27] The current wording may exclude the viewpoints of key stakeholders, such as family members or caregivers who also have exposure and experience with the treatment that does not fall under the current specifications.

- Therapeutic Impact on Specific Populations: Although CMS is directed in the IRA to consider comparative effectiveness of a drug and therapeutic alternatives, CMS goes further in Question 41 to state that the Agency will consider "therapeutic impact" on "specific populations." CMS should provide additional detail on what this entails or use and clearly define an alternative term.

- Safety Profile: In seeking information about the range of impacts of a selected drug and its therapeutic alternative(s) for the purpose of comparative effectiveness research, the ICR should substitute the current terminology "Safety Profile" with "Benefits and Risks" in Question 41 to ensure CMS is collecting information on the full range of information on each product. The current language is too narrow to capture the information we believe CMS is seeking through this question as basic safety profiles on comparators can be pulled from labels,

- Cost: "Cost" should be more clearly defined under Question 41 to include a consideration of a range of direct and indirect costs (such as the costs to caregivers, transportation costs, lost work time), and cost savings associated with appropriate use of a selected drug. Furthermore, to ensure an even comparison between the selected drug and any therapeutic alternatives, the cost considered should reflect the true net cost after rebates to Medicare including accounting for any significant discounts provided under the 340B Drug Pricing Program. In order to make sure CMS receives appropriate and comparable information from this question, CMS

[26] Berger ML, Sox H, Willke RJ, et al. (2017). Good Practices for Real-World Data Studies of Treatment and/or Comparative Effectiveness: Recommendations from the Joint ISPOR-ISPE Special Task Force on Real-World Evidence in Health Care Decision Making. Value in Health. 20(8):1003-1008.

[27] Patient-Centered Outcomes Research Institute's Advisory Panel on Patient Engagement. (2021). Equity and Inclusion Guiding Engagement Principles. PCORI. Available at: https://www.pcori.org/about/pcoris-advisory-panels/advisory-panel-patient-engagement/equity-and-inclusion-guiding-engagement-principles.

should also clarify what documentation or citations are required to support any provided cost figure(s).

- Unmet Medical Need: CMS' definition of "unmet medical need" in Question 43, which is defined as, "A drug or biologic that treats a disease or condition in cases where very limited or no other treatment options exist is considered to meet an unmet medical need[,]" is too narrow. As mentioned in Section III.f. of our Guidance comments, CMS should at a minimum expand this definition to meet the FDA's definition of unmet need.[28] However, CMS should also explicitly recognize other types of unmet needs including, but not limited to: 1) personalized medicines for certain subpopulations; 2) progress against rare and hard-to-treat illnesses; 3) treatments that improve patient adherence and quality of life; 4) need for additional treatments in a therapeutic area, such as a curative treatment; 5) treatments that improve the health of underserved and vulnerable communities who face health disparities; 6) treatments that benefit multiple common comorbidities at once; 7) populations and individuals failing to meet established treatment guideline goals from available therapies and; 8) the stepwise nature of progress in which significant gains for patients are achieved via advances that build on one another. To ensure CMS is able to fully assess whether or not a treatment addresses an "unmet" need, CMS should broaden and clarify its definition.

- Comparative Effectiveness: CMS should strive to accept all valid and rigorous methodologies that tell the value story. To do this, the Agency should clarify what is acceptable as appropriate comparative effectiveness including acceptance of indirect treatment comparisons (including non-head-to-head trials), and pre- or post-treatments comparisons.

- Therapeutic Alternatives: As noted in Section III.c. of our Guidance comments, experts, including manufacturers and clinicians, should be the primary resources for determining therapeutic alternative(s). The Agency should be clear that if data submitters choose to provide information on therapeutic alternative(s), the therapeutic alternative(s) should not only include drugs indicated for the same disease or condition as the selected drug, but also those that are similarly used in clinical practice.

- Therapeutic Impact: In question 41, "Therapeutic Impact and Comparative Effectiveness" the first bullet states "Please provide information on the therapeutic impact of the selected drug compared to existing therapeutic alternatives." As therapeutic impact can extend beyond comparative effectiveness, the Agency should confirm that they will accept information on therapeutic impact within healthcare system as well as comparative effectiveness.

Transparency for Manufacturers of Selected Drugs

CMS should provide transparency and visibility as to how it will conduct its review of the evidence and provide further guidance on whether this information obtained will be disclosed to manufacturers and other data submitters. Further, the Agency should publicly describe the process it will use to obtain information for clinical and subject matter experts through mechanisms other than the ICR, and how this information will be made available to the public and/or manufacturers participating in the MFP process. Upon review, CMS should make publicly available the non-proprietary data it gathers under Section (e)(2) on alternative treatments and should share information with the manufacturers of selected drugs and therapeutic alternatives as quickly as possible.

[28] FDA. (2014). Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. Available at: https://www.fda.gov/files/drugs/published/Expedited-Programs-for-Serious-Conditions-Drugs-and-Biologics.pdf

Technical Improvements:

CMS currently provides a list of six categories of respondents (*e.g.*, representative of a manufacturer that does not manufacture the selected drug, representatives of a secondary manufacturer of the selected drug, etc.) under Question 39. CMS should make significant revisions to this list both to revise the descriptions of the stakeholders listed, and to list a broader range of stakeholders that will be interested in providing information. First, CMS should broaden the descriptions of the stakeholder categories it does identify. In particular, it should revise the description of health care providers and patients to extend beyond those with direct experience prescribing or taking a medicine and include those who otherwise have expertise or knowledge about the drug.

CMS also should expand the list of stakeholders to avoid creating the impression that submissions from some members of the public are not sought or valued by the Agency. This should include creating a category for "representatives of organizations representing patients, people with disabilities, family caregivers or consumers" that is separate from the "trade association" category. Further, in other documents related to the ICR (CMS' Guidance document and the Supporting Statement for the ICR itself), CMS identifies other categories of relevant stakeholders, and the Agency should ensure these, and other stakeholders are included on this list. For example, the ICR Supporting Statement lists "patients and consumers, Part D plan sponsors and Medicare Advantage organizations, Primary Manufacturers, manufacturers of therapeutic alternatives for a selected drug, hospitals and health care providers, wholesalers, pharmacies, researchers, and other members of the public" that "may provide additional insight into selected drugs and alternative treatments." CMS should ensure that the stakeholder list on Question 39 is at least as detailed and comprehensive as the list in the Supporting Statement.

Finally, CMS should also allow clinicians to indicate if they are a clinical expert in the field (e.g., specialist) and should make sure respondents can indicate if they are a caregiver, payor, or any other party with significant interest in the impact of the price setting process.

In the text containing the instructions for Questions 40 through 43, the sixth bullet, "When citing studies to support responses, briefly summarize the study context and relevant comparator or therapeutic alternative drug(s) studied, as applicable" is repeated as the eighth bullet. For clarity, CMS should remove one repeated bullet and once again explicitly state that this is optional as summarizing a study could be viewed as burdensome to patients, providers, and their representatives which could deter them from responding to the ICR.

The ICR "Questions to Respond to for Question 41" and "Questions to Respond to for Question 42" reflect the important role that comparative effectiveness data will play in the MFP decision-making process, and the very limited window of time that manufacturers will have to submit this data. In this context, it will be important for manufacturers to have more timely access to CMS' claims and prescription drug event files for conducting real-world analysis, particularly given that the Agency has indicated it may conduct their own real-word evidence analyses, and these may entail use of the same data sets. Under CMS' current policy on claims data access, it is not possible for manufacturers (or many other important stakeholders) to have ready access to CMS medical claims and prescription drug event files. Access to the CMS Research Identifiable data requires following the processes set forth by the Research Data Assistance Center (ResDAC). Requests to RedDAC require detailed descriptions of proposed analyses, can be rejected by ResDAC for any number of reasons, and the process for gaining data access is likely to exceed the time window afforded to a manufacturer (a month from notification to submission). As a result, CMS should either create a new mechanism for manufacturers to access CMS Research Identifiable data in order to conduct comparative effectiveness research or certify that they will not use mechanisms not available to manufacturers to access CMS Research Identifiable data. In addition, if CMS intends to conduct their own RWE studies, the process should be transparent and provide opportunities for manufacturers and other key stakeholders to review study designs and provide input.

Question 42, which asks about comparative effectiveness on specific populations, should include text boxes to allow respondents to identify key benefits and risks of the selected drug and therapeutic alternatives on specific populations.

As noted above, CMS should remove the word limits for responses in the entire ICR. These arbitrary limits may force data submitters to cherry pick data instead of providing a balanced view on the totality of evidence. The word and citation limits are especially concerning in Section H for the questions related to therapeutic alternatives because the ICR provides a very limited number of questions and data fields while seeking information that encompasses multiple treatment options, multiple indications, and large volumes of evidence on a wide range of clinical and patient-centered outcomes that have accumulated through years of post-approval research.

Based on the large volume and variety of data that may be available on the questions in Section H, CMS should provide additional fields for submission of data on specific indications and outcomes throughout the section. The Agency should also include an open text box at the end of Section H to allow for the submitter to include other information that was not captured in the previous questions but that is still important for CMS consideration. In addition, CMS should accept attachments and other sources of data to support the narrative provided. These could include, but are not limited to, tables, statements, and other sources of information that may not be able to be provided within a citation. Any such materials should be shared with the selected manufacturer as soon as possible.

VI. Certification of Submission

The ICR requires all respondents to certify that the information submitted is "complete and accurate."[29] Respondents must also agree to notify CMS in a timely manner upon becoming aware "that any of the information submitted in this form has changed[.]"[30] According to the terms of this certification, any misrepresentations may give rise to liability, including under the False Claims Act.

We first note that nothing in the statute requires a certification as proposed by CMS. This contrasts with other provisions in the Social Security Act, which specifically require such certifications. For example, section 1124(c)(3)(A) requires the Secretary to promulgate regulations for disclosure of ownership and other information that ensure that "the facility certifies, as a condition of participation and payment under [Medicare and Medicaid], that the information reported by the facility . . . is, to the best of the facility's knowledge, accurate and current."

CMS should modify the certification to delete the requirement to certify to "completeness," unless the Agency provides further guidance on the definition of "complete." As discussed previously, given the age, history, and preexisting retention policies, manufacturers may not be able to access all relevant records and thus may not be able to certify "completeness." Therefore, without additional guidance on what data and information qualify as "complete," particularly within the "Evidence About Alternative Treatments" portion of the ICR, stakeholders are beholden to a vague standard of certification on an open data set that may lead to legal risks. Furthermore, given the existing word limits, submitters may not be able to submit complete answers to some of the questions. Stakeholders should instead certify only that their submitted information is accurate.

CMS should remove the requirement of timely notification of changed information to avoid unintended noncompliance of the certification and unnecessary burden. The scientific field continues to evolve with new publications and disclosures. As a result, this term of the certification, with no specification of the applicability of a time limit, adds an ongoing burden for all submitters that CMS suggests could lead to legal liabilities and consequences.

[29] CMS, ICR Form at 42-43.
[30] *Ibid.*

PhRMA is further concerned that, as drafted, the certification statement may prevent manufacturers from submitting evidence that relies on disclosed assumptions or estimates where necessary, due to the timeline of data collection and issues with data collection previously discussed in this letter.

PhRMA urges CMS to remove the liability clause in the certification. Instead, CMS should mirror the Average Sales Price Data (Addendum B) certification, which requires only that the information was submitted "in good faith" and reflects the submitter's best "knowledge and belief."[31]

Additionally, PhRMA is concerned that the certification requirement could create an unnecessary barrier for data submission by many external stakeholders that is not imposed in other CMS decision-making contexts such as coverage determinations or provider fee schedule changes. In particular, CMS should not require patient groups or patients and caregivers, responding in their individual capacity, to sign any certification whatsoever. In addition, CMS should monitor submissions of evidence under (e)(2) to determine the extent to which certification may create a barrier for some stakeholders.

VII. Burden Estimates and Information Collection Burden

CMS has invited comment on both the burden estimates and the use of automated collection techniques or other forms of information technology to minimize the information collection burden. CMS' calculations provide an estimate that each manufacturer will likely spend 500 hours at a cost of $51,588.50 to respond to the data request. This is a severe underestimate for reasons that include the following:

- CMS proposes to collect a vast amount of data, in a new program, under an aggressive timeline, with potentially extreme penalties associated with the collection. Companies are thus likely to assign full or partial FTEs to the price submission requirements and hire consultants and/or law firms to advise on submissions and corresponding assumptions.

- CMS has requested data in a manner that is unfamiliar and unclear to manufacturers, such as CMS splitting one statutory R&D category into seven sub-categories, requiring many hours from manufacturers to collect, allocate, and report data with very little clear benefit. CMS should account for the extreme burden and cost of this approach. The R&D category alone will likely absorb more than the total 500 hours CMS estimates for the ICR.

- There is also the additional burden to collect and search for historical data, such as historical R&D data, that could be non-existent or maintained within older internal systems that are difficult to access.

- The manner in which CMS requests the information is not how manufacturers collect these data. As a result, collecting data – such as at an NDC-9 level – or converting units between alternate standards – will be highly burdensome and will vastly increase the monetary and time burdens required by manufacturers to comply.

- While PhRMA urges CMS to abandon its primary/secondary manufacturer policy, if CMS finalizes the policy, it will only exacerbate and increase the Primary Manufacturer's burden.

- Collecting the CER factor information and evidence about alternative treatments will be a significant burden, both for the manufacturer of the selected drug and other stakeholders, as this research is not currently collected or submitted to CMS.

[31] CMS. (rev'd 2018). Average Sales Price Data Certification Form (Addendum B). Available at: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/downloads/aspdata_addendumb.pdf

CMS also states that manufacturers have experience providing information similar to the negotiation factors set forth in Sections 1193(a)(4)(A) and 1194(e) based on manufacturer submission of data to other entities, such as: the Securities and Exchange Commission (SEC); CMS as a result of the Medicaid National Drug Rebate Agreement; and States through negotiations for supplemental rebates. PhRMA, however, is not aware of any entity (public or private) that collects data at the excruciating level of detail CMS proposes in its ICR. States, the SEC, and private entities allow companies to report data in broader terms (such as overall R&D on a company-wide basis) and to offer reasonable assumptions. They also do not present the same level of risk, given the significant CMPs and excise taxes potentially at issue.

Further, CMS should have calculated some level of burden for collection and submission of information on comparative effectiveness, cost, and unmet need under Section 1194(e)(2). For reasons described above, many manufacturers of selected drugs, as well as other stakeholders including manufacturers of potential therapeutic alternatives, likely will feel compelled to submit information under (e)(2) due to the nature of the MFP process. The Agency is remiss in not giving any consideration to information collection burden under this section in its estimate.

VIII. Conclusion

PhRMA appreciates the opportunity to submit comments in response to the *Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act.* We urge CMS to limit the data that must be provided to elements essential to operation of the Program; leverage data already available to them as much as possible; and provide additional time for supplemental data submission. Please contact James Stansel at jstansel@phrma.org and/or Jennifer Bryant at jbryant@phrma.org if there is additional information we can provide or if you have any questions about our comments.

-----s-----
Jennifer Bryant
Executive Vice President
Policy, Research, and Membership
PhRMA

----s-----
James C. Stansel
Executive Vice President and General Counsel
PhRMA

May 22, 2023

Via Electronic Filing: http://www.regulations.gov

William N. Parham
CMS, Office of Strategic Operations and Regulatory Affairs
Division of Regulations Development
Attention: CMS-10847, OMB Control No.: 0938-NEW
Room C4-26-05
7500 Security Boulevard
Baltimore, Maryland 21244-1850

Re: Information Collection Request for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB 0938-NEW)

Dear Mr. Parham:

Sanofi US ("Sanofi" or "Company") appreciates the opportunity to provide comments on the Centers for Medicare & Medicaid Services' ("CMS'") *Information Collection Request ("ICR") for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act ("IRA")* (CMS-10847, OMB 0938-NEW) (hereinafter the "ICR"), including the Federal Register Notice, ICR Form, and Supporting Statement – Part A (CMS-10847, OMB, 0938-NEW).[1]

Sanofi brings together world-class research and development in pursuit of leading health care solutions that serve several major therapeutic areas including vaccines, diabetes, chronic kidney disease, multiple sclerosis, cardiovascular disease, oncology, rare diseases, immunology, hemophilia, and over-the-counter (OTC) products. We are committed to discovering, developing, and making available to patients and their treating physicians innovative, effective, well-tolerated, and high-quality treatments that fulfill vital health care needs.

Sanofi appreciates CMS' efforts to solicit comments on its proposed ICR and to allow manufacturers and other interested parties to provide feedback on CMS' proposed approach to collecting data regarding the selected drugs under Medicare Drug Price Negotiation Program (the "Program"), established by the Inflation Reduction Act (P.L. 117-169). Sanofi supports the comment letters submitted by Pharmaceutical Research and Manufacturers of America ("PhRMA") and Biotechnology Industry Organization (BIO), and this letter is intended to supplement those comments.

As described in more detail below, Sanofi's comments and recommendations are as follows:

- Sanofi strongly supports and echoes the following concerns in the PhRMA comment letter regarding: (1) the highly confidential nature of the requested information; (2) the 31-day timeframe in which manufacturers must collect this information, which is far too short to gather and submit a complete response; and (3) the breadth of information

[1] 88 Fed. Reg. 16,983. (Mar. 21, 2023). *Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)*, CMS (Mar. 21, 2023), https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847 ("ICR Form"); *Information Collection Request (ICR) for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10847, OMB 0938-NEW)*, Supporting Statement – Part A, CMS, https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847 ("Support Statement – Part A").

requested that in some cases exceeds the scope of the statutory factors and in other cases is cut too narrowly so that it does not accurately capture the full scope of a manufacturer's investment in the drug research, development, and distribution processes. Sanofi also believes that CMS significantly underestimates the burden of this ICR. It will take far longer than 500 hours for manufacturers to collect relevant data and draft responses in the requested format.[2]

- Sanofi urges CMS to place greater weight on the clinical value of a selected drug, rather than input cost-based factors when developing the Maximum Fair Price ("MFP") offer or evaluating a manufacturer's counteroffer. Prioritizing cost-recovery would significantly harm incentives for research and development, undermine efforts to discover medicines that address unmet need, and is inconsistent with CMS' goal of transitioning Medicare toward a value-based care and payment.

- Section C. Research & Development ("R&D") Costs and Recoupment. The ICR arbitrarily excludes certain categories of R&D costs and requests R&D costs in ways that may not reflect the full scope of time and financial investment that go into R&D efforts. We also are concerned that CMS' approach suggests that CMS may weigh certain R&D activities inappropriately. Specifically, Sanofi recommends that CMS take a more holistic approach to collecting and considering R&D costs associated with an active moiety/ingredient, which would more accurately reflect how manufacturers fund R&D. We also suggest CMS allow manufacturers the ability to attest if they have recouped their R&D costs.

- Section D. Unit Costs of Production and Distribution. CMS' proposed definition of distribution does not accurately reflect the significant costs that go into drug distribution. In addition to marketing costs, which are covered in a separate section, Sanofi incurs other costs related to distribution, such as patient affordability and support programs and costs related to various overhead and other functions, such as sales, finance and accounting, legal, human resource, regulatory, medical, and quality. Sanofi recommends that CMS allow manufacturers more discretion in providing cost data that is broadly related to product distribution.

- Section E. Prior Federal Financial Support. It can be difficult and time-consuming to identify prior Federal financial support. Thus, CMS should allow some leeway for manufacturers to submit information that manufacturers can obtain based on good faith effort.

- Section G. Patents, Exclusivities, and Approvals. The intellectual property protections enshrined in the US patent system are the pillar of this nation's innovation engine that drives our ongoing success in discovering life-saving and innovative medicines and vaccines. CMS' approach to considering patents and other exclusivities should be consistent with the policy objectives of that system to reward and protect innovation. In other words, CMS should not downwardly adjust the MFP on the basis of the selected drug's remaining patents and exclusivity. Additionally, to the extent CMS appropriately considers patents related to a selected drug, it should place little consideration on pending patent applications as those are subject to amendment during the US Patent & Trademark Office ("USPTO') review process and may never be issued. Finally, Sanofi strongly encourages CMS to minimize the burden on manufacturers by seeking publicly available patent and exclusivity information directly from its sister agencies whenever possible.

- Section G. Market Data, Revenue, and Sales Volume Data. CMS should utilize price reporting metrics that are already established and available to CMS, such as Average Manufacturer Price and Average Sales Price. Requiring manufacturers to report new pricing metrics, which are not clearly defined, would result in confusion and inconsistent data that is of limited utility to CMS. Similarly, CMS should leverage existing Non-

[2] *See* Supporting Statement – Part A, § B.12, CMS.

Federal Average Manufacturer Price ("NFAMP") data reported to the Veteran's Administration rather than make manufacturers report slightly different NFAMP data. Finally, CMS should not consider prices that were statutorily-defined for specific purposes, such as the 340B Ceiling Price, which is intended to support access to certain vulnerable patients.

- Section H. Evidence About Alternative Treatments. Sanofi strongly recommends that CMS identify all therapeutic alternatives that CMS intends to rely on concurrently with, or as soon as possible after, publishing the list of selected drugs. Given the central role of therapeutic alternatives in establishing the "starting point" for the MFP, it is important that CMS provide stakeholders with notice and an opportunity to comment on potential therapeutic alternatives. Further, CMS should remove the proposed word counts and citation limits and permit manufacturers to submit information on a rolling basis, so that stakeholders can provide CMS with a holistic understanding of the value of a selected drug and its therapeutic alternatives.

Our detailed comments and specific recommendations on the ICR's data questions are provided in detail below.

I. When Considering the Statutory Factors in Determining Maximum Fair Price Offers and Counteroffers, CMS Should Give Primary Consideration to the Drug's Value

Sanofi announced its commitment to sustainable pricing through its progressive and industry-leading principles. Sanofi's responsible approach to pricing reflects its medicines' value, and its commitment to patient access and to minimizing the Company's contribution to health care inflation.

Sanofi holds itself to a rigorous and structured process, that includes consultation with external stakeholders, when it sets the price of a new medicine. The Company's approach considers the following factors:

- A holistic assessment of value, including 1) clinical value and outcomes, or the benefit the medicine delivers to patients, and how well it works compared to standard of care treatments; 2) economic value, or how the medicine reduces the need—and therefore costs—of other health care interventions; and 3) social value, or how the medicine contributes to quality of life and productivity. Sanofi's assessments rely on a range of internal and external methodologies, including health technology assessments ("HTAs") and other analyses that help define or quantify value and include patient perspectives and priorities.

- Similar treatment options available or anticipated at the time of launch, in order to understand the landscape within the disease areas in which the medicine may be used.

- Affordability, including the steps Sanofi must take to promote access for patients and contribute to a more sustainable system for payors and health care systems.

- Unique factors specific to the medicine at the time of launch. For example, Sanofi may need to support ongoing clinical trials to demonstrate the longer-term outcomes of our medicines, implement important regulatory commitments, or explore opportunities to improve care management/patient experience and help decrease the total cost of care.

Similarly, when establishing the MFP for the selected drug, Sanofi strongly encourages CMS to place primary emphasis on the value-related factors set forth in Section 1194(e)(2) of the SSA ("Evidence About Alternative Treatments"). Even if CMS improves the scope and approach to collecting manufacturer-specific data (set forth in Section 1194(e)(1) of the SSA), consistent with PhRMA's and Sanofi's recommendations, we continue to believe those considerations should be secondary to the value that a medicine provides to patients and society more broadly.

II. Section C. Research & Development Costs and Recoupment

A. Research & Development Costs Requested in the ICR Do Not Accurately Reflect the Investment that Goes into Drug Research & Development

Section C of the ICR proposes to collect "dollar amounts for [R&D] and recoupment costs . . . and [] explanations of how those costs were calculated."[3] CMS proposes to define R&D costs, generally, to mean a "combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug" that fall into the following categories: Basic Pre-Clinical Research Costs, Post-Investigational New Drug ("IND") Application Costs, Completed FDA-Required phase IV Trials, Post-Marketing Trials, Abandoned and Failed Drug Costs, and All Other R&D Costs.[4]

In several recent years, Sanofi spends approximately $7 billion on R&D, pursuing best-in-class and first-in-class therapies and vaccines that have the potential to transform the practice of medicine and improve patients' lives. But, like other companies in our industry, only a small fraction of the molecules we research become approved medicines or vaccines. On average, it takes 10-15 years and costs $2.6 billion to develop one new medicine, including the cost of the many failures.[5] In fact, only 12% of new molecular entities that enter clinical trials eventually receive FDA approval.[6] Given the significant financial risks and rate of failure, manufacturers consider R&D budgets holistically across their entire pipeline and often establish drug development programs that explore a molecule's potential across different potential indications. CMS should take the same holistic approach when considering a manufacturer's R&D costs. Collecting R&D data related primarily to indications approved by the FDA provides an inaccurate and incomplete view of R&D investment of a particular molecule and more broadly leaves out significant additional investment in R&D of other molecules that failed prior to FDA approval.

Sanofi is concerned that the ICR too narrowly defines a manufacturer's R&D costs. For example, Questions 1 through 4 are expressly limited to R&D costs associated with the FDA-approved indications. Further, the ICR limits R&D costs for failed or abandoned efforts (Question 5) to a portion of "direct basic pre-clinical research on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials" and "post-IND costs for drugs within the same therapeutic class as the selected drug that did not achieve FDA approval."[7]. While CMS provides a catch-all question for all other R&D costs (Question 6), which presumably could include failed or abandoned R&D projects associated with unlabeled indications or in other therapeutic areas, it is not clear that CMS will consider these costs with the same weight as the other categories. Sanofi believes that CMS should equally consider all of a manufacturer's R&D costs without imposing arbitrary distinctions. Given the high failure rate and associated financial risks of pharmaceutical innovation,[8] CMS should give manufacturers credit for all of their R&D investments, not only the subset that ultimately led to FDA-approved indications.

Sanofi is also concerned that the ICR arbitrarily and without explanation expressly excludes any R&D costs associated with ongoing basic pre-clinical research, clinical trials, and pending approvals.[9] These ongoing research efforts are no less worthy of consideration as they reflect, per the statute, "research and development costs of the manufacturer for the drug," and may constitute efforts to learn more about the safety or efficacy of the drug for existing patient populations and/or extend the benefit of the drug to new patient populations through additional regulatory approvals.

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[3] Section C, ICR Form, at 5.
[4] Section C, ICR Form, at 5.
[5] Rick Mullin, *Tufts Study Finds Big Rise In Cost Of drug Development*, Chemical & Engineering New (Nov. 20, 2014), https://cen.acs.org/articles/92/web/2014/11/Tufts-Study-Finds-Big-Rise.html#:~:text=A%20new%20report%20published%20by,the%20center%20made%20in%202003.
[6] Research and Development in the Pharmaceutical Industry, Congressional Budget Office (April 2021), https://www.cbo.gov/publication/57126.
[7] Section C, ICR Form, at 11.
[8] D. Sun et al., *Why 90% of clinical drug development fails and how to improve it?*, 12 APSB 7, at 3049-62 (July 2022), https://www.sciencedirect.com/science/article/pii/S2211383522000521.
[9] Section C, ICR Form, at 5.

Omitting these costs provides an incomplete picture of a drug's development and discounts the significant investment that manufacturers make to discover and develop medicines and vaccines.

In sum, Sanofi strongly encourages CMS to collect more holistic information about a manufacturer's R&D costs, including the past and ongoing R&D costs, irrespective of whether the research was ultimately successful. Without these changes, the current ICR dismisses other important R&D efforts that contributed to a selected drug's discovery and development as well as future discovery and innovation efforts.

B. Manufacturers Will Face Numerous Challenges to Retrieve and Timely Submit the Requested Research and Development Cost Data

Through prior experience trying to identify and collect comprehensive R&D data related to particular drugs, Sanofi knows that complying with this request will be extremely burdensome and difficult to complete within the short timeframe requested. It would be difficult for manufacturers to obtain older R&D financial data for products that may have passed through a number of corporate entities within the Primary Manufacturer and/or may be contained in retired data repository systems.

Sanofi urges CMS to recognize the challenges to obtaining R&D data set forth in Section C of the IRA, let alone within the 30-day timeframe. Rather than requesting data that certain manufacturers may not have based on their unique circumstances, CMS should allow manufacturers the flexibility to attest whether they have recouped their R&D costs by answering a check box YES or NO. If the answer is Yes, no other data should be required. If the answer is NO, a free form text box with information about why the answer is NO should be supplied. The R&D format created by CMS to provide costs in six categories[10] with explanations is overly burdensome and may be nearly impossible to accomplish in the limited time period required. Instead, we ask CMS set forth a reasonable approach that is both fair and realistic especially in the early years of this program. In time, both parties will become more adept at developing the most efficient and effective reporting systems. For now, we believe a free form text box with explanations is the place to start. Additionally, an over emphasis on R&D costs to set price is fundamentally flawed. We urge CMS to consider the value of the medicine and not put too much weight on a cost-plus pricing model.

III. Section D. Unit Costs of Production and Distribution

Section D of the IRC require manufacturers to submit current unit costs of production and distribution for the selected drug.[11] In particular, CMS requires manufacturers to submit "[a]llocated shared operating and other indirect costs specific to each NDC-9 based on unit volume."[12] Current units costs exclude R&D costs and marketing[13] costs.

CMS' proposed definition of distribution costs is unnecessarily narrow and does not account for many other expenses associated with selling and distributing medicines, including the expenses associated with, for example, patient affordability and other support programs associated with the selected drug. Additionally, the definition does not account for the significant overhead expenses associated with distributing drugs in the marketplace, such as sales, finance and accounting, legal,

[10] (1) basic pre-clinical research for all approved indications of the selected drug; (2) post-IND costs for all approved indications of the selected drug; (3) costs of all completed, Food and Drug Administration (FDA)-required Phase IV studies for the selected drug; (4) costs of all post-marketing trials for the selected drug; (5) costs of failed or abandoned products related to the selected drug; and (6) costs of other R&D for the selected drug not accounted for in the preceding categories

[11] Section D, ICR Form, at 14-15.

[12] Section D, ICR Form, at 15.

[13] Sanofi supports the plain language definition of marketing provided in the ICR ("'marketing' is defined as the introduction or delivery for introduction into interstate commerce of a drug product." ICR Form, at 3) and strongly recommends that CMS utilize this definition throughout the Program. CMS' decision to interpret "marketing" in the Initial Program Guidance dated March 15, 2023 is far too complicated and subjective, and is not supported by the statute. *See Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*, CMS (Mar. 15, 2023), https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf ("Initial Program Guidance").

human resource, regulatory, medical, quality, and other functions. These costs are generally not allocated product-by-product. Sanofi strongly recommends that CMS broaden its definition of distribution to encompass these types of additional direct and indirect costs, the components of which could be disclosed in response to Question 9 explaining the methodology.

IV. Section E. Prior Federal Financial Support

Section E of this ICR would require manufacturers to report prior Federal financial support for "novel therapeutic discovery and development."[14] "Federal financial support" is defined to include "tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and/or development of the drug."[15] "Prior Federal financial support" could either be for such support issued during the "time period from when the initial research began [], or when the drug was acquired by the Primary Manufacturers, to the day through the date the most recent NDA/BLA was approved for the selected drug."[16]

Manufacturers may face significant challenges in obtaining information regarding prior Federal financial support for the selected drug. Given the breadth and complexity of the information that CMS requires, Sanofi strongly encourages CMS to allow manufacturers to submit information based on the manufacturer's good faith attempt at gathering such information.

V. Section F. Patents, Exclusivities, and Approvals

Section F of the ICR would require manufacturers to submit data related to "pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the [FDA] or section 351(a) of the Public Health Service Act."[17] CMS further defines "patents" relevant to this Section F to include "all pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired by the Primary Manufacturer . . . ."[18]

Patents are a constitutionally-granted form of intellectual property protection that provide inventors the exclusive right to make, use, or sell their inventions for a certain period of time.[19] The USPTO may grant a patent after an extensive technical review, if the invention is "new and useful"[20] and "non-obvious."[21] The patent application process is a long and arduous process that takes approximately two years on average.[22] More than 85% of patent applications are rejected at least once, and when rejection happens, the applicant must amend the claims of the application, which define with particularity what would be covered by the patent should it eventually be granted, without any guarantee of future success.[23] The U.S. patent system is crucial to pharmaceutical innovation and medical advancement as it promotes competition and provides critical incentives for innovation.[24]

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[14] Section E, ICR Form, at 16.
[15] Section E, ICR Form, at 16-17.
[16] Section E, ICR Form, at 17.
[17] Section F, ICR Form, at 19.
[18] Section F, ICR Form, at 19.
[19] U.S. Const. art. I, § 8, cl. 8.
[20] 35 U.S.C. § 101
[21] 35 U.S.C. § 103.
[22] Patent Help – Application Processes – Technical Information – Other, USPTO, https://www.uspto.gov/help/patent-help#type-browse-faqs_1208 (last visited May 16, 2023) ("Currently, the average patent application pendency is 24.6 months.").
[23] PhRMA, "Megan Van Etten, *IP Explained: How does the U.S. patent process work?* Pharmaceutical Research and Manufacturers of America (June 24, 2021), https://catalyst.phrma.org/ip-explained-how-does-the-u.s.-patent-process-work."
[24] Ian Cockburn & Genia Long, *The importance of patents to innovation: updated cross-industry comparisons with biopharmaceuticals*, Expert Opinion on Therapeutic Patents, 25:7, 739-42 (2015), https://doi.org/10.1517/13543776.2015.1040762 ("Due to distinctive economic characteristics, patents and regulatory exclusivity have long been considered essential to prescription drug development. These characteristics include the costly, lengthy, and risky nature of innovative research and development (R&D) and the much lower

Yet, Section F of this ICR and CMS's Initial Program Guidance would have the opposite effect, as they would *penalize* manufacturers for obtaining patent protections. Specifically, under Section 60.3.4 of the Initial Program Guidance, CMS states that "if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward."[25] CMS' planned approach to considering patents and exclusivities undermines the intent for such intellectual property protections and penalizes manufacturers for doing the very thing that makes our nation the industry leader—*i.e.*, discovering and patenting new drug discoveries and related technologies

We also recommend that CMS place lesser weight on patent applications because such applications are subject to change or may never be granted. Moreover, these pending patent applications (such as provisional patent applications) include highly confidential information that are not published for a certain period of time.[26] It is unreasonable for CMS to give weight (particularly negative weight) to the potential intellectual property protections associated with a patent application before it is finalized or approved. As currently proposed, CMS' approach disincentivizes manufacturers from investing in new innovation, which could only lead to fewer new drugs to address unmet medical needs.

Finally, CMS should consult publicly-available sources and only request that manufacturers report information that is not available to the Agency. This is consistent with the Paperwork Reduction Act ("PRA") requirement that agencies should take "every reasonable step to ensure that the proposed collection of information is not duplicative of information otherwise accessible to the agency."[27] For example, CMS should consult FDA's Purple Book and Orange Book for information on approved patents for the drug rather than requiring manufacturers to report this information.

VI. Section G. Market Data, Revenue, and Sales Volume Data

Section G of the ICR goes far beyond CMS's statutory authorization to require manufacturers of selected drugs to report "[m]arket data and revenue and sales volume data from the drug in the United States."[28]

Section G would require manufacturers to respond to Question 17 through 38. Some questions seek data that CMS already has available.[29] For example, CMS already collects Average Manufacturer Price and Best Price as part of the Medicaid Drug Rebate Program and, as CMS acknowledges, there are public databases that provide wholesale acquisition prices for drugs. Consistent with PRA requirements, CMS should not require manufacturers to resubmit this data.[30]

Other questions in this section seek data on newly-concocted pricing metrics that are not clearly defined, have limited incremental utility over already-available data, and arguably exceed CMS's statutory authority. Sanofi opposes CMS's proposal to require reporting of new pricing metrics: US Commercial Average Net Price (Questions 31 and 32) and Manufacturer Average Net Unit Price to Part D Plan Sponsors (Questions 33 and 34). For each of these pricing metrics, CMS seeks the price with patient assistance programs, without patient assistance programs, and "best" (e.g., "the lowest U.S. commercial average net unit price offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S." and "the lowest manufacturer average net unit

investment required for generic drugs. Because of this disparity, without patent protection and regulatory exclusivity, particularly in the USA, innovators would be unlikely to make the substantial investments required to bring new drugs to market.").

[25] Initial Program Guidance at 53.

[26] *See, e.g.*, 35 § U.S.C. 122(a) ("Except as provided in subsection (b) [(e.g., after the expiration of a period of 18 months from the earliest filing date for which a benefit is south under this title)], applications for patents shall be kept in confidence by the Patent and Trademark Office and no information concerning the same given without authority of the applicant or owner unless necessary to carry out the provisions of an Act of Congress or in such special circumstances as may be determined by the Director.").

[27] 5 C.F.R. § 1320.5(d)(1)(ii).

[28] Section G, ICR Form, at 24.

[29] Section G, ICR Form, at 24-38.

[30] 5 C.F.R. § 1320.5(d)(1)(ii).

price to Part D Plan sponsors offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any Part D plan sponsor").[31] Sanofi is concerned that these new pricing metrics are vaguely defined, likely leading to uncertainty for manufacturers and inconsistent data that will be of limited utility to CMS. Sanofi strongly encourages CMS to withdraw these new pricing metrics and instead rely on existing pricing metrics and financial data manufacturers already report in their financial disclosure filings.

Similarly, under Section B of the ICR, CMS states that it will require manufacturers to report the NFAMP of each NDC-11 for the selected drug for each calendar quarter of calendar year 2021.[32] As PhRMA noted in its Initial Program Guidance comment letter dated April 14, 2023, CMS should utilize the annual NFAMP that manufacturers calculate and report to the VA.[33] Specifically, while CMS intends to use the NFAMP of each NDC-11 for the selected drug for each quarter of calendar year 2021, the VA already defines an annual NFAMP as a weighted average across the four quarters of the federal fiscal year (*i.e.*, October to September of the following year).[34] CMS should not create a new annual non-FAMP calculation, and instead should use the existing annual NFAMP based on the fiscal year, as reported to the VA.

Finally, certain data that CMS proposes to collect under Section G, such as 340B Ceiling Price, 340B Prime Vendor Program Price, Federal Supply Schedule Price, and Big Four Price, are inappropriate considerations when establishing the MFP because they are statutorily-mandated prices intended for specific categories of patients – not the Medicare population. For example, the 340B Ceiling Price is a statutorily set price intended to permit entities that treat a disproportionate percentage of low-income patients to access drugs at lower costs.[35] Further, the 340B statute specifically provides that "the manufacturer offer each covered entity covered outpatient drugs for purchase at or below the applicable ceiling price if such drug is made available to any other purchase at any price."[36] Nowhere in the statute states that manufacturers must extend the 340B Ceiling Price to those other than covered entities. Utilizing these deep discounted prices as one of the benchmark prices for MFP also could disincentivize manufacturers from continuing to participate in programs that help vulnerable patients.

VII. Section H. Evidence About Alternative Treatments

Section H of the ICR allows Primary Manufacturers and other interested parties to voluntarily submit information on the selected drug's therapeutic alternative(s).[37]

As described above, Sanofi believes that CMS should give greater weight to the value-related factors, as described under Section 1194(e)(2) of the SSA. Focusing on the cost-related factors is inconsistent with Medicare's efforts to transition to value-based care and payment. Moreover, this approach would significantly harm incentives for R&D and undermine efforts to discover future medicines that address unmet needs.

Additionally, Sanofi strongly recommends that CMS publicly identify the therapeutic alternative(s) that CMS intends to use as part of the Program. As currently proposed, stakeholders would not know the therapeutic alternative(s) that CMS intends to consider at the time of the ICR submission, and even worse, stakeholders cannot provide any feedback on CMS' choice of the therapeutic alternative(s) after the ICR submission. Sanofi's recommended approach would allow

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[31] Section G, ICR Form, at 25-26.
[32] Section B, ICR Form, at 4.
[33] *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments*, Pharmaceutical Research and Manufacturers of America, at 59-60 (Apr. 13, 2023), https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/G-I/PhRMA-Comments-on-CMS-Initial-Guidance-on-Medicare-Drug-Price-Negotiation-Program22948.pdf.
[34] *See* 38 U.S.C. § 8126(h)(5).
[35] *See* 42 U.S.C. § 256b.
[36] 42 U.S.C. § 256b(a)(1).
[37] Section H, ICR Form, at 38.

stakeholders to study CMS' proposition and provide any feedback on CMS' selected therapeutic alternative(s) in addition to any information stakeholders wish to provide on proposed therapeutic alternative(s) to a selected drug.

CMS currently imposes word and citation limits that prevent manufacturers from providing sufficient data and evidence in response to the questions posed under each section. Sanofi urges CMS to remove the word and citation limits from all sections, but particularly from Section H, in which CMS is seeking extensive data that could encompass multiple treatment options, indications, and large volumes of data.

Sanofi also strongly encourages CMS to accept data from stakeholders on a rolling basis, including after October 2, 2023. Sanofi is concerned that many key stakeholders, including from the patient and provider communities, may not be able to submit responses within the proposed month-long timeframe.

* * * *

Sanofi hopes CMS finds these comments helpful and will incorporate our recommendations into its revised ICR. We also hope that CMS will reflect our recommendations in the revised Program guidance and implement the Program in a way that it minimizes the Program's potential to disincentivize pharmaceutical innovation. If you have any questions, please do not hesitate to contact me (liz.cirri@sanofi.com 202-412-1513).

Sincerely,

/s/

Liz Cirri
Head Public Policy and Reimbursement
Sanofi, US Corporate Affairs