June 12, 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 Drug Price Negotiation Process Under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10849, OMB 0938-NEW)

Dear Mr. Parham:

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 also work to solve 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.

AstraZeneca appreciates this opportunity to comment on the Centers for Medicare & Medicaid Services' (CMS') proposed information collection request (ICR) for the Drug Price Negotiation Process Under Sections 11001 and 11002 of the Inflation Reduction Act (IRA). This document describes the information collection, via CMS's proposed "Counteroffer Form," that may occur during the negotiation process if the Primary Manufacturer chooses to develop and submit a written counteroffer to CMS's written initial offer during the drug price negotiation process for initial price applicability year 2026.

As described in greater detail below, AstraZeneca recommends that CMS take the following steps to improve the quality, utility, and clarity of the information collected using the Counteroffer Form, while minimizing burden on the Primary Manufacturer:

- Expressly authorize participation in the counteroffer process by Secondary Manufacturers.
- Provide a sufficient justification for CMS's initial offer to enable manufacturers to respond to CMS's justification using the Counteroffer Form. In particular, given the importance of therapeutic alternatives to the application of the negotiation factors specified in section 1192(e)(2) of the Social Security Act (the "Act"), we urge CMS to include a concise justification for the specific therapeutic alternatives used in applying the section 1194(e)(2) factors, to include the evidence CMS relied upon to select those therapeutic alternatives, the potential therapeutic alternatives the Agency considered and did not select, and the evidence the Agency considered in rejecting such therapeutic alternatives.
- Take steps to protect proprietary and confidential information submitted via the Counteroffer Form.

- Expand the Counteroffer Form's data fields to permit the submission of additional information.

I. CMS Should Expressly Authorize Participation in the Counteroffer Process by any Secondary Manufacturers.

In the ICR, the proposed Counteroffer Form is described as applicable only to the Primary Manufacturer, which CMS defines the holder of the New Drug Application (NDA) or Biologics License Application (BLA) for the selected drug. We are concerned this approach—combined with CMS's proposed limitations on the use and disclosure of information specific to the negotiation process—may impose undue burden on the Primary Manufacturer and interfere with the collection of useful information by CMS.

While there are often multiple manufacturers associated with the development, production, and distribution of a drug, the distinction between a "Primary Manufacturer" and a "Secondary Manufacturer" does not exist in statute. Rather, this concept was established by CMS in the initial guidance for the Medicare Drug Price Negotiation Program (the "Negotiation Program").[1] In that guidance, CMS also proposed to prohibit the Primary Manufacturer from disclosing to the public: (1) any information in the initial offer or any subsequent offer by CMS; (2) the ceiling price contained in any offer; (3) any information contained in any concise justification provided with an offer; or (4) any information exchanged verbally during the negotiation period.

The application of CMS's proposed data restrictions to the exchange of data between the Primary Manufacturer and any Secondary Manufacturers would interfere with CMS's ability to obtain important information regarding selected drugs via the Counteroffer Form and otherwise. Specifically, where multiple manufacturers are involved with a given drug, each of the manufacturers may have unique information and perspectives regarding the drug and its value, all of which should be considered for purposes of the Negotiation Program regardless of which manufacturer owns the NDA/BLA. However, it would be burdensome, and in some cases impossible, for the Primary Manufacturer to complete the Counteroffer Form without being able to share information regarding the negotiation process with Secondary Manufacturers. AstraZeneca therefore recommends CMS clarify that its proposed data restrictions—if finalized—in no way restrict a Primary Manufacturer from coordinating with any Secondary Manufacturer(s) to complete the Counteroffer Form.

II. CMS's Justification for its Initial Offer Must be Sufficient to Enable Manufacturers to Respond.

In the ICR, CMS proposes that the Primary Manufacturer would provide: (1) a written counteroffer for the MFP per 30-day equivalent supply of the selected drug; (2) a justification of the counteroffer based on the section 1194(e) factors: and (3) a response to the justification provided in CMS's initial offer including why the information submitted by the manufacturer on the section 1194(e) factors does not support the written initial offer made by CMS and better supports the manufacturer's counteroffer.

As a threshold matter, we note it is difficult to provide informed comments on the burden associated with completing the Counteroffer Form because we have yet to see what details CMS intends to provide in its justification for the initial MFP offer. Along those lines, AstraZeneca strongly urges CMS to provide sufficient detail in its initial offer to enable manufacturers to consider the adequacy of the initial offer, as well as whether CMS's justification for the offer is appropriate. While we appreciate the statute refers only to a "concise justification" for the initial offer, CMS must ensure there is sufficient information in the initial offer to facilitate due process and to improve the quality, utility, and clarity of information collected in the Counteroffer Form. At a minimum, the initial offer should include information regarding each of the following:

- How CMS weighed each of the factors in section 1194(e) of the Act, as applicable to the drug, and the adjustments made by CMS to the starting point using each such factor.
- Specific data sources consulted and relied upon by CMS in weighing each of the section 1194(e) factors and why.
- The therapeutic alternatives identified by CMS for purposes of applying the section 1194(e)(2) factors, including the evidence the Agency relied upon to select those therapeutic alternatives, the potential therapeutic alternatives the Agency considered and did not select, and the evidence the Agency considered in rejecting such therapeutic alternatives.
- Any section 1194(e) factors CMS found inapplicable to the drug and why.
- How CMS calculated the MFP for a 30-day equivalent supply.
- How CMS proposes to weight the initial offer across dosage forms and strengths.

III. CMS Should Take Steps to Protect Proprietary and Confidential Information Submitted via the Counteroffer Form.

AstraZeneca supports CMS's recognition in the ICR that the information collected through the Counteroffer Form may contain proprietary, trade secret, or other confidential information. However, to provide manufacturers certainty that any sensitive information disclosed via the Counteroffer Form will be sufficiently protected, we would appreciate greater clarity regarding the procedures CMS will use to protect such information from unauthorized use or disclosure in a manner consistent with the requirements of section 1193(c) of the Act. In addition, as we previously commented in response to the initial Negotiation Program guidance, CMS should provide manufacturers of selected drugs with the opportunity to review any reported data in advance of publication, including as part of the explanation for the MFP as required under section 1195(a)(2) of the Act, to ensure that no competitively sensitive information is disclosed to the public.

IV. CMS Should Expand the Data Fields in the Counteroffer Form to Permit the Submission of Additional Information.

AstraZeneca is concerned the Counteroffer Form, as currently drafted, would not permit a Primary Manufacturer to provide a sufficient rationale or adequate documentation for its counteroffer. There are also certain aspects of how CMS describes use of the Counteroffer Form which appear inconsistent with the version of the Counteroffer Form included in the PRA package.

To improve the quality, utility, and consistency of the information collected, and to ensure the Counteroffer Form can achieve its intended purpose, AstraZeneca recommends CMS amend the Counteroffer Form to include each of the following:

- Fields to submit the manufacturer's methodology for calculating the equivalent 30-day supply, as well as how the manufacturer's MFP counteroffer is weighted across dosage forms and strengths, if different from the methodologies used by CMS.
- A field to append supplemental data sources and files needed to rebut CMS's initial offer justification and to provide support for the manufacturer's counteroffer, which may require data beyond that initially submitted by the manufacturer in response to the negotiation data elements ICR.
- A field for signature by the authorized representative of the Primary Manufacturer.
- A field for countersignature by CMS in the event CMS agrees to the counteroffer.
- A field for the manufacturer to request that certain details contained in the Counteroffer Form be included in the public explanation for the agreed-upon MFP for the selected drug (unless CMS intends to use a separate form/process for this purpose, which should be explained in the final negotiation program guidance and/or updated Counteroffer Form).

V. Conclusion

AstraZeneca thanks you for the opportunity to submit comment regarding the ICR and look forward to continuing to engage with CMS as it implements the Negotiation Program for IPAY2026 and beyond. I can be reached at sarah.arbes@astrazeneca.com with any questions.

Sincerely,

Sarah Arbes
Head, U.S. Federal Government Affairs & Policy

Cc: Lara Strawbridge, Deputy Director for Policy, Medicare Drug Rebate and Negotiations Group at the Center for Medicare

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202-962-9200

June 20, 2023

Via Electronic Delivery
The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-10849
7500 Security Boulevard
Baltimore, MD 21244-1850

RE: Information Collection Request (ICR) for the Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849)

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 the counteroffer process 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.

It is Difficult to Respond to the Counteroffer Process When We Do Not Yet Know What the Initial Offer and Justification Will Look Like nor Has CMS Released the Draft Negotiation Agreement for Review

In soliciting feedback on the Counteroffer process, CMS is perplexingly soliciting feedback on a part of an overall process that has not yet been released. It is, quite frankly, near impossible for stakeholders to provide substantive feedback on the counteroffer process when we do not know what the initial offer and justification will look like. Even more fundamentally, CMS has not made the negotiation program agreement available for public comment. CMS has said it will make "reasonable efforts" to make the final text of agreement available to the public before the first selected drug publication date. It is imperative that CMS make the text of the agreement available for public comment and do so well in advance of when manufacturers will be required to execute the agreement.

CMS should provide manufacturers with a confidential report during the initial offer process to show the evidence they used in establishing the initial offer, how they evaluated said evidence, alongside a detailed explanation of each factor they weighted. Manufacturers should have the ability to review that justification in the confidential report, and it should be more detailed than what reports CMS might make public facing. However, CMS should also work to release some guidance on how it will approach its initial justification, so manufacturers who are selected are better able to work ahead of time to understand the Agency's approach.

Without any modicum of information as to what the initial justification for the offer will be, responding to the ICR seems to be a futile exercise. In withholding information on its approach for an initial justification and the overall "negotiation" process from key stakeholders, the Agency does nothing to assuage the fears of patients and manufacturers that this process is nothing but government price setting.

At the outset of the process of implementing the IRA, CMS said that it would work with manufacturers and other stakeholders to incorporate their feedback into the process that the Agency would eventually establish. CMS has left stakeholders unable to provide any actual comprehensive feedback on various aspects of the process by keeping the overall "negotiation" process behind a black box. This black box approach in turn makes CMS look to be nodding through its pre-planned process without having to adjust its predetermined approach by having to incorporate feedback from manufacturers and other stakeholders.

We have been urging CMS to release information on the overall "negotiation" process in a timely manner in order to allow for substantive and meaningful engagement with stakeholders. While we continue to believe that a transparent process with opportunity for stakeholder review and feedback is the most appropriate approach, we note that CMS is running out of time to allow for such an approach. At this juncture it appears that the Agency is operating with limited

transparency in implementing its preplanned process, to the detriment of patients, manufacturers, and the future of American biopharmaceutical innovation.

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.

Moreover, with just one day provided between the deadline to submit the agreement for "negotiation"—which we reiterate is not an actual negotiation process, but rather government price setting— and the deadline for when materials are due to be submitted to CMS, the ability to submit pertinent data that may arise after a timely submission is critical. This ICR on the counteroffer process does not highlight any way in which supplemental information can be provided in advance of, or even during, the counteroffer process.

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 provide 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. There is no reason why CMS should make this "counteroffer" process more difficult than it has to be.

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. CMS is planning to rely on new metrics that need to be reported, such as the US commercial average net unit price, and not price reporting metrics 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 and make the "counteroffer" process smoother.

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 question asking for the justification of the manufacturer's counteroffer, which has a word limit of only 1,500 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. 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 for the counteroffer, not limiting the response to just the negotiation factors in sections 1194(e). 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 12 (with table 1) attached, CMS estimates the burden to be 79 hours per Primary Manufacturer per selected drug at a base estimate cost of $9,987.01 per manufacturer per drug. [1] We believe these numbers are dramatic underestimates of the actual cost in time and money for each submitting manufacturer in creating a robust counteroffer.

In particular, the difficulty a manufacturer will have in crafting a counteroffer is further exacerbated by the as-yet unreleased initial justification for the initial offer. If the initial justification does not get released until the initial offer is released to manufacturers, manufacturers will have to work to both comprehend CMS's rationale for the offer and suitably address it in their statement (which is already constrained by arbitrary word limits).

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

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 CMS as part of the negotiation process. In addition, BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers, as well as CMS's mandate to "destroy" evidence of the negotiation process.

[1] Counteroffer Process ICR Supporting Statement at 8.

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,"[2] 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,[3] will apply to information to be submitted under the program.[4] We continue to 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[5] 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.[6] CMS should ensure that similar controls are in place with respect to HPMS, given CMS's intent to transition most information submissions to that system.

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[2] Initial Guidance at 29.

[3] *See* 45 C.F.R. §§ 5.41, 5.42.

[4] Counteroffer Process ICR Supporting Statement at 4.

[5] 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).

[6] CMS, *Medicaid Drug Programs User Manual* 1 (Nov. 3, 2021).

CMS should also specify how it will maintain the confidentiality of the subset of information that is required to be submitted via Box. With regard to Box (a third-party commercial platform), BIO asks CMS to specify how submitted information will be kept confidential, including against misuse by Box personnel.

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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

June 20, 2023

VIA ELECTRONIC FILING - WWW.REGULATIONS.GOV

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
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Attn: PO Box 8016

Re: Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849, 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 Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849, OMB, 0938-NEW). 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 to Regulations.Gov

June 20, 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: Drug Price Negotiation Process ICR

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 Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)* ("Drug Price Negotiation Process 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. For these reasons, BMS has filed a federal lawsuit asking a court to declare the IRA unconstitutional. 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. Although our comments are designed to help CMS in these areas as it implements the process that Congress established in the IRA, nothing we say in this comment letter should be construed as suggesting that CMS can cure the constitutional flaws in the statute that Congress wrote.

[1] 88 Fed. Reg. 23,680 (April 18, 2023); CMS, "Information Collection Request (ICR) Form for Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10849, OMB 0938-NEW)," *available at* https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10849.

The IRA will have vast ramifications for patients, providers, manufacturers, and other stakeholders across the country. BMS is concerned that CMS' implementation of the IRA could have sweeping negative repercussions with respect to Medicare beneficiary access to needed medicines, and, indeed, for *all* patients. It is vital for CMS to give meaningful consideration of and response to stakeholder feedback on its proposals.

BMS believes that it is essential for CMS to develop and finalize a process that allows stakeholders to reasonably predict how price setting will operate in practice. Any "negotiation" under the IRA should include full transparency regarding stakeholders' comments and CMS' interpretation and evaluation of such comments. BMS urges CMS to commit to a process without arbitrary limitation on the scope of such dialogue (*e.g.*, through limitation of meetings and/or limitations on "counteroffer" 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 Drug Price Negotiation Process ICR. As with our comments to the recently released Medicare "Negotiation" Guidance,[2] 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.

Key comments include:

- **Initial Written "Offer":** BMS is concerned that CMS' proposed process by which the Agency will determine an "offer" will de-value pharmaceutical advancements that are currently on the market and result in even greater chilling effects on future innovation. BMS is also concerned that the descriptions of certain calculations in the Guidance lack sufficient clarity and introduce certain ambiguities that may make it challenging for manufacturers to follow the methodology and accurately replicate calculations for selected products.
- **"Counteroffer" Process:** BMS strongly believes that CMS should meet with the manufacturer of a selected medicine at *multiple points* during the "negotiation" process to allow manufacturers to address questions and provide additional commentary on the value of these medicines. While we agree with CMS that meetings after any rejection of a manufacturer's "counteroffer" are necessary and will allow for a more efficient and effective process, initiating meetings with manufacturers only after such rejection is too late. BMS also asks CMS to remove the 1500-word limit on a manufacturer's justification of its "counteroffer" (the "Free Response" in Question 3).
- **Confidentiality:** BMS believes 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.

I. Initial Written "Offer"

BMS believes that it is essential that stakeholders be able to reasonably predict how the determination of a "Maximum Fair Price" ("MFP") will operate in practice. We note that it is *especially* important that CMS be fully transparent regarding the "negotiation" and "renegotiation" methodology and process. BMS appreciates CMS sharing initial high-level thoughts in the Guidance, but we believe that additional details are needed, with an opportunity for stakeholders

[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.

to have full visibility into the methodology and process, as well as the opportunity to provide comment on such forthcoming details to better inform the parameters.

a. Price Setting Process

BMS is concerned that CMS' proposed process by which the Agency will determine an "offer" will de-value pharmaceutical advancements that are currently on the market and result in even greater chilling effects on future innovation. To limit the harm to patient access to innovation, BMS generally believes that CMS should always set the "MFP" at or near the "MFP" ceiling—that is, the higher of the sum of the plan specific enrollment weighted amounts or the applicable percent of the nonfederal average manufacturer price (non-FAMP)—for each selected product. BMS also urges CMS to carefully consider situations where issues of patient access or preservation of incentives for innovation demand that a selected drug should be paid at the "MFP" ceiling. To help limit the harm to patient access, BMS recommends that, at a minimum, CMS set all "MFPs" at the "MFP" ceiling price for initial price applicability year (IPAY) 2026. Should CMS choose *not* to set prices at the "MFP" ceiling price for all selected medicines, we recommend that CMS give special consideration to setting the "MFP" at the ceiling price in the following circumstances: (1) when patient access is especially imperiled; (2) for IPAYs into which patent protection exists; (3) for small molecule parity; (4) for preference on medical guidelines; and (5) for when states reference the "MFP".

BMS understands CMS' desire to convert utilization across a medication's dosage forms and strengths into a consistent 30-day equivalent supply. While this methodology may yield a meaningful metric for certain Part D drugs which are exclusively in tablet form, taken at a consistent rate through the entire course of therapy, not approved for varying regimens to treat different indications, and not prescribed uniquely to each patient based on their own individual body weight or other personal characteristics, it is important for CMS to recognize that many products do not meet all of these criteria, which will preclude establishment of a single price that can be applied meaningfully to all national drug codes (NDCs).

Moreover, at a threshold level, CMS' calculation methodology takes an additional, unnecessary step that is contrary to the statutory requirement of the Agency to "establish[] procedures to compute and apply the ['MFP'] across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug."[3] Specifically, CMS proposes to apply the "MFP" ceiling twice—a first time at the drug level, and a second time at the dosage form or strength level. CMS should not—and, indeed, may not—finalize this proposal.

The statute defines both the "MFP" and the ceiling price as a price determined at the drug level. Nowhere does the statute contemplate the application of the ceiling price at the dosage form or strength level. The statute directs CMS to establish a process to apply the "MFP"—which already has been capped by the ceiling price—to each dosage form and strength of the selected drug, and it does not authorize the application of the ceiling price a second time. And as a factual matter, such double application could cause the "MFP" of some dosage forms and strengths of a selected drug to be reduced a second time. A wholesale acquisition cost (WAC) ratio for a dosage form or strength higher than 1.0 could generate a dosage form/strength-level "MFP" that is above the dosage form/strength-level ceiling price—and thus a dosage form/strength-level "MFP" that is doubly capped. This double capping would unfairly penalize dosage forms and strengths with a higher WAC ratio, even though such higher WAC ratio could merely reflect a difference in utilization, such as a difference in dosing regimen or a higher Part D utilization.

[3] SSA § 1196(a)(2).

Beyond the threshold statutory issue with CMS' proposed calculation methodology, additional notable challenges with using a 30-day equivalent supply for pricing include: weight-based dosing; dosing variations across indication; and dosing titration/loading doses/changes in dosing over course of treatment.

BMS is concerned that the descriptions of certain calculations in the Guidance lack sufficient clarity and introduce certain ambiguities that may make it challenging for manufacturers to follow the methodology and accurately replicate calculations for selected products. To provide greater clarity, we urge CMS to provide example calculations for illustrative drugs. These calculations should be representative of complex situations, such as weight-based based dosing or dosing variations across indications. Clarity in CMS' calculations will help ensure there is sufficient predictability in how CMS will interpret and apply these complex methodologies.

b. Provision of an Initial "Offer" and Justification

It is critical for manufacturers to understand the context and basis for the "MFP" "offer". To increase transparency and further CMS' two-way dialogue with a manufacturer of a selected drug, we urge the Agency to consider releasing a confidential report for the manufacturer alone alongside the initial "offer" and justification to better inform manufacturer "counteroffers" and subsequent data submissions. Ex-U.S. markets with longstanding value assessment experience extend greater flexibility to and collaboration with manufacturers, including transparency during the decision-making process. Given the anticipated submissions from members of the public, including academic experts and clinicians, CMS will have a significant amount of information on a selected drug, as well as latitude in determining what is included in an initial concise justification. Manufacturers are unlikely to have enough context to effectively address potential evidence gaps. We therefore ask the Agency to provide a confidential report to manufacturers with details on the Agency's assessment of a selected product, as well as the evidence which was deemed relevant and appropriate from stakeholder submissions. The concise justification and report should, at a minimum, include the following information: (1) evidence sources CMS considered, including third-party assessments the Agency may have formally or informally considered; (2) how each factor was weighted in CMS' "MFP" determination; (3) how patients and other stakeholders engaged in the process and influenced CMS' decision-making; and (4) benefits and impacts that CMS considered.

II. "Counteroffer" Process

BMS has serious concerns with CMS' process for interfacing with manufacturers of selected drugs. While we agree with CMS that meetings after any rejection of a manufacturer's "counteroffer" are necessary and will allow for a more efficient and effective process, initiating meetings with manufacturers only after such rejection is too late. In our vast experience with negotiating with states and payers, the proposed process would be highly unusual and arbitrary, and would not even approximate a true negotiation—which, for instance, does not feature limitation on engagement between parties, in contrast with CMS' contemplated limitation to three meetings. Other countries have adopted a more collaborative approach with manufacturers and have implemented a process that encourages a high frequency of contact between the health technology assessment (HTA) agency and manufacturers to resolve questions and outstanding issues.

In fact, the importance of an open dialogue between the U.S. government and industry in a negotiation process has long been recognized. For general federal procurement, for example, early exchanges of information prior to acquisition are encouraged, as such exchanges "can identify and resolve concerns regarding the acquisition strategy, including proposed contract type, terms and conditions, and acquisition planning schedules; the feasibility of the requirement, including performance requirements, statements of work, and data requirements; the suitability of the proposal instructions and

evaluation criteria, including the approach for assessing past performance information; the availability of reference documents; and any other industry concerns or questions."[4] The Federal Acquisition Regulation (FAR) suggests that the mechanism for this exchange can include one-on-one meetings with potential offerors, industry conferences, and public hearings. Oral presentations by offerors can also occur at any point in the acquisition process and "provide an opportunity for dialogue among the parties."[5] For pharmaceutical negotiations specifically, both the Department of Veterans Affairs (VA) and Department of Defense (DoD) commonly utilize two-way discussions prior to any formal federal decision/implementation of medication management. Based on examples found elsewhere related to government negotiations, BMS asserts that CMS should, at a minimum, create a more open and transparent "negotiation" with manufacturers without any additional artificial limitations other than those required by statute.

BMS strongly believes that CMS should meet with the manufacturer of a selected medicine at *multiple points* during the "negotiation" process to allow manufacturers to address questions and provide additional commentary on the value of these medicines. At a minimum, we urge CMS to meet with manufacturers during six discrete periods in the value assessment process—but without limitation on the number of meetings deemed necessary by the parties: (1) prior to drug selection; (2) after drug selection but prior to initiation of the "negotiation" process; (3) immediately after manufacturer data and evidence submissions; (4) prior to CMS presenting initial "MFP" "offer"; (5) after CMS presents the initial "offer"; and (6) after a "counteroffer" is made.

III. Completing the "Counteroffer" Form

a. Instructions for Completing the "Counteroffer" Form

The Medicare Negotiation Guidance introduced the concept of "Primary Manufacturers" and "Secondary Manufacturers". The Drug Price Negotiation Process ICR affirms such terms, noting that the Primary Manufacturer is responsible for developing and submitting a written "counteroffer", among other duties. BMS does not agree with the "Primary Manufacturer" 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 certain 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.

b. "Counteroffer" Form

BMS strongly encourages CMS to remove the 1500-word limit on a manufacturer's justification of its "counteroffer" (the "Free Response" in Question 3). Practically speaking, given the complexity and amount of information likely shared related to a selected product, a 1500-word limit is insufficient for a manufacturer to provide a meaningful justification for a "counteroffer". Manufacturers may also want to convey "counteroffer" information through tables and/or charts, but that format does not appear to be permitted with the proposed text format. This limitation is also arbitrary. When submitting a "counteroffer" to the Agency, there should neither be limitations on file sizes nor transmission options. Many experienced HTA markets with long established frameworks do not impose word limits on submission dossiers. We ask CMS to extend the maximum flexibility to manufacturers to share important evidence on and rationale for the values of our medications in the most appropriate format for the manufacturer and the selected product.

[4] Federal Acquisition Regulation (FAR), Part 15 - Contracting by Negotiation, 15.201(c) Exchanges with industry before receipt of proposals.
[5] *Id.* at 15.102(a) Oral presentations.

IV. Other Comments

a. Confidentiality

BMS agrees with CMS that the Agency should ensure that 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. BMS also asks CMS to carefully consider how the Agency intends to keep confidential commercial information confidential within the Agency itself.

Confidentiality Safeguards with Respect to the Public Explanation of the "MFP": BMS notes that it benefits all parties—including CMS—if the Agency openly discloses the informational assumptions that it relies upon in developing "offers" and responses. By disclosing the informational basis of such "offers" and responses, CMS will facilitate a more open and transparent dialogue during the "negotiation" process. For example, manufacturers will be able to better understand CMS' positions and rationales and thereby tailor more appropriate "counteroffers" and replies. Furthermore, open disclosure of the non-manufacturer-submitted information upon which CMS relies will reduce the risk of CMS' "offers" and responses reflecting a misunderstanding or misinterpretation of such information—because manufacturers will be in a position to raise any such errors or misapprehensions to the Agency's attention.

While supportive of transparency in "MFP" "offers" and "counteroffers", BMS is concerned about the potential for improper disclosure of confidential commercial information when CMS publishes the statutorily-required explanation of the "MFP" for a selected drug.[6] We ask that CMS expressly confirm that, in publishing the explanation for the "MFP", it will ensure that trade-secret, proprietary, and other confidential commercial information will not be directly or indirectly disclosed.

Furthermore, BMS believes that a manufacturer should be permitted to identify for CMS any way in which the intended explanation of the "MFP" would reveal confidential commercial information. To help ensure that such information will not be inadvertently disclosed, we ask CMS to afford the manufacturer a reasonable opportunity to review and raise confidentiality concerns regarding CMS' intended explanation of the "MFP", in advance of its publication.

Data Use Provisions and Limitations: We oppose CMS' proposals to restrain manufacturer speech in relation to information acquired during the "negotiation" process. We also oppose the proposal to mandate destruction of manufacturer property (*i.e.,* the "destruction of data"). Among other things, these unprecedented proposals violate the First Amendment and run contrary to principles of fairness, transparency, and accountability. The proposals should be withdrawn, and CMS should engage stakeholders regarding appropriate and lawful measures to impose in connection with data use.

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[6] SSA § 1195(a)(2).

BMS appreciates the opportunity to comment on the 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

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

CLL SOCIETY

VIA ELECTRONIC DELIVERY

April 14, 2023

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

RE: Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026

Dear Administrator Brooks-LaSure:

CLL Society appreciates the opportunity to submit its comments on the Centers for Medicare & Medicaid Services' (CMS') Initial Guidance on implementation of the Drug Price Negotiation Program created under the Inflation Reduction Act of 2022 (IRA).

CLL Society is dedicated to addressing the unmet needs of 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. We are the largest nonprofit focused exclusively on the unmet needs of patients living with CLL and SLL.

We strive to fulfill our primary mission of ensuring 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 providers and patients. As an organization, we also recognize that the healthcare landscape extends beyond science, clinical care, and patient support. Legislative, regulatory, and policy initiatives have the potential to exert a considerable and increasing force on equitable access to existing treatments and the development of new therapeutic options.

CLL Society expects that the IRA provisions capping Part D out-of-pocket costs will bring substantial relief to our patient community. Just as importantly, CMS' implementation of a "smoothing" mechanism will allow patients to spread their out-of-pocket costs over the year and avoid the all-too-common scenario of having to base treatment decisions on their financial concerns rather than their medical needs.

While the drug price negotiation program may have a marginal impact on healthcare costs for patients with relatively common conditions, as well as CLL and SLL patients who are not currently receiving active treatment, it will likely have no impact on out-of-pocket costs for patients requiring

active therapy. There is little doubt that the decisions CMS makes now on the price negotiation program will become part of the complex calculations researchers, investors, and drug manufacturers make when determining whether to pursue a particular drug candidate for a specific indication. We fear that without a proactive intent to preserve the fragile cost/benefit balance in small population diseases, CMS will inadvertently tip the scales away from innovation in CLL and SLL as well as other related blood cancers.

Our comments provide a brief background on the disease and focus on the potential impact that the policies and processes within CMS' Initial Guidance might have on our patient community. We urge CMS to exercise its implementation discretion to ensure that our health system continues to welcome the rapid scientific advances in our understanding of disease mechanisms and targeted treatment approaches that have driven 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 21,000 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 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 yet located in the bloodstream. When the cancer is only found in the lymph nodes it is called SLL. When the cancer is found in the bloodstream and possibly elsewhere, including lymph nodes, it's called CLL.

CLL/SLL is extremely heterogeneous, meaning each person's disease course and progression can be extremely variable. Some experience rapid deterioration due to having an aggressive form of the disease and survive for as little as two years, while some who have a less aggressive form of the disease will never need treatment and 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 our patient community. Patients now have more treatment options compared to just years ago when the standard of care was chemoimmunotherapy. They can take continuous daily oral therapy with a BTK inhibitor, with or without a monoclonal antibody, until their disease progresses. Alternatively, patients can choose a short-term time-limited treatment approach that combines venetoclax and a monoclonal antibody. The latter approach enables dose discontinuation until active monitoring reveals that another 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, and many are forced to either change treatments, take a "drug holiday," or adjust dosing due to drug intolerance. For patients with relapsed or refractory disease (or treatment 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 can experience serial relapses, and many will be treated with all available agents at some point during their disease course.

The unfortunate reality is that despite significant progress in treating CLL/SLL, it remains an incurable cancer. Patients progressing after both BTK and BCL2 inhibitors 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. Manufacturers have voluntarily withdrawn indications for idelalisib in both follicular lymphoma (FL) and SLL, and duvelisib in FL. Additionally, umbralisib was completely withdrawn from the market. The FDA's recent ODAC meeting recommended the withdrawal of duvelisib. If this comes to pass, there will be no available PI3K inhibitor approved as a single agent in CLL, and none at all in SLL.

The experience with PI3K inhibitors in CLL/SLL illustrates the inherent difficulties surrounding studying this disease and the heightened risk manufacturers take on when pursuing new therapeutic candidates. Delays associated with the wait for overall survival data have already dampened research efforts and slowed patient access to potentially life-saving therapies. We have advocated for crossover in clinical trials to save lives, but the strategy inherently compromises the "purity" of survival data. Since CLL/SLL is not an ideal disease state from a research perspective, "new" treatments are often first approved for other cancers and then later approved for CLL/SLL under FDA's accelerated approval mechanism. Research and development efforts in CLL/SLL could be significantly deterred due to the combination of increased payer hesitance to fully cover and pay for accelerated approval therapies, and the likelihood that a CLL/SLL indication would render an existing drug ineligible for the IRA orphan exclusion to price negotiation, slowing new drug development in CLL/SLL and other rare cancers. We are concerned that this evolving landscape, viewed holistically, poses dire consequences for CLL/SLL patients as they exhaust available treatment options.

CMS should extend the time for stakeholder feedback on the Initial Guidance.

CLL Society has reviewed the complex set of policies within the Initial Guidance with an eye toward identifying concerns within our patient and provider communities and making recommendations to address those concerns. We had hoped that CMS would fulfill its commitment to prioritize transparency and robust engagement in implementing the price negotiation program. Unfortunately, CMS has issued "final" guidance to implement policy decisions we did not anticipate in light of the statutory language, that importantly warrant public input and will likely drive the success or failure of the program. To the extent that CMS reached out to the patient advocacy

community in advance of issuing the Initial Guidance, we were unaware of the approach CMS was considering, much less the opportunity to shape alternative approaches.

We are also concerned that the Agency exposes itself to legal challenges that will inject considerable uncertainty among manufacturers, investors, and even private payers. Uncertainty is a highly disruptive force that can stall or deter access to the resources that fuel innovation. We urge CMS to consider stakeholder feedback received through the 30-day comment process and extend the time for additional comments on the entirety of the Initial Guidance. Going forward, we also respectfully request that CMS develop a review process that allows for a consistent and open dialogue with the patient community. For the countless patients hoping for new treatments and equitable access to existing options, the stakes are too high for CMS to prioritize expedience over inclusion and consideration.

Orphan Drug Exclusion

CLL Society appreciates CMS' interest in stakeholder ideas that might facilitate orphan drug development. We also generally support the Agency's decision to extend the orphan drug exclusion to drugs with a single designation (as opposed to a single indication). The small and emerging biotechnology companies responsible for over 80% of orphan product development are particularly vulnerable to landscape changes that can impact the recoupment of research and development costs.

The risk/benefit analysis is particularly complex within the context of CLL/SLL treatments. 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 in 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 January 19, 2023, announcement that FDA had approved zanubrutinib for both CLL and SLL was particularly significant in that it worked well in patients with difficult-to-treat cancers (i.e., those with a mutated gene called TP53, or a chromosomal alteration known as a 17p deletion). We believe it is unlikely that the manufacturer would have invested in the studies required for this set of approvals if its label expansion would have rendered the drug ineligible for the orphan drug exclusion.

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 approved for CLL/SLL and expect a response. This is because once a drug within that same drug class has failed the patient, all drugs within that same class will likely fail. The January 27, 2023, accelerated approval of reversibly binding BTK inhibitor pirtobrutinib for the treatment of mantle cell lymphoma was a significant advance in lymphoma treatment, as it is

indicated for relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, ***including a BTK inhibitor.*** This treatment has already demonstrated the potential to address a significant unmet need in CLL/SLL patients who have been failed by an irreversibly binding BTK inhibitor. We are pleased that Eli Lilly is moving forward with their clinical trials in CLL, and our patient communities are hopeful that these studies will result in an FDA-approved treatment for patients who have exhausted their existing options. As the drug price negotiation program becomes a tangible reality for manufacturers, however, there is a very real danger that it will drive decisions on the drug candidates and/or indications manufacturers and investors are willing to pursue.

The sets of incentives encouraging the development of treatments for small-population diseases have generally worked well to expand treatment options and improve survival for patients with CLL/SLL and other blood cancers. The IRA's narrow exclusion for orphan drugs, however, creates a landscape in which multiple designations for a promising therapy will negate eligibility for the exclusion, thereby substantially complicating analyses on the potential for favorable return on investment. Manufacturers may face pressures to focus on an orphan indication with the largest patient population rather than the disease state that is most suitable for clinical trials. This could impact the time it takes to move a product from bench to market, increase costs associated with securing a first approval, and deter studies in Waldrenstrom's Macroglobulinemia and other blood cancers with extremely small patient populations.

We are similarly concerned that manufacturers will face considerable tension between their legal and fiduciary obligations to shareholders and their perceived moral obligation to cancer patients. Any decision to invest in research toward an expanded label that could ultimately disqualify the drug from the orphan drug exclusion would appear to be unsupportable if the follow-on indication population is small. Manufacturers may also face difficulties securing approval from their directors, shareholders, and investors to continue confirmatory studies for accelerated approval indications with small addressable populations if withdrawing those indications would make a drug eligible for the orphan drug exclusion. We do not believe Congress or the Administration sought to limit research and development in orphan diseases generally or in rare cancers. Manufacturers secured orphan designations well before the IRA was enacted and could not have considered that a relatively narrow designation would later drive consequences to research and development in other indications.

We believe researchers, investors, and manufacturers should be rewarded, not penalized, for investing in research and development to secure FDA approval for new indications (rather than relying on off-label use). It would be a tremendous tragedy if Congress' efforts to improve healthcare affordability created an environment in which future treatments like Pirtobrutinib would never be indicated for CLL/SLL (or mantle cell lymphoma) despite their potential to transform patient care. These concerns are compounded by the fact that the same considerations exist for other treatments with orphan designations outside CLL/SLL. Zanubrutinib, for example,

was first approved in 2019 for mantle cell lymphoma. Its MCL approvals, as well as the label expansion in relapsed or refractory marginal zone lymphoma (MZL), were granted through the accelerated approval mechanism and remain contingent upon the completion of confirmatory studies. Zanubrutinib's orphan designation is for mantle cell lymphoma, and each additional indication is outside that narrow designation, including the label expansions for CLL/SLL and WM that were secured through FDA's traditional approval mechanism. CLL Society expects that the IRA will make approval histories like that of Zanubrutinib a thing of the past, despite the significant benefit conferred to blood cancer patients from manufacturer-sponsored studies in multiple indications.

CLL Society asks that CMS support and pursue Congressional action to remove the single orphan designation/indication requirement for orphan drug exclusion eligibility. The statutory language as it stands leaves manufacturers with a no-win proposition and jeopardizes patient access to promising therapies without any benefit to the Medicare program or society as a whole. We also urge CMS to implement a stop-gap measure through its demonstration authority that would maintain the status quo with regard to payment mechanisms (e.g., ASP-based), and apply to orphan drugs that do not have annual utilization in any one indication that exceeds 200,000 patients.

In addition, we urge CMS to enable manufacturers to submit evidence demonstrating eligibility for the orphan drug exclusion.

Definition of Qualifying Single Source Drug

CLL Society urges CMS to reconsider its decision to identify a qualifying single source drug, and its dosage forms and strengths, by referring to common active moiety (drugs) or common active ingredient (biologics). The approach that CMS has chosen is not mandated by the statutory language. In fact, the IRA appears to require that products be treated as the same qualifying single-source drug only when they share an NDA or BLA. The determination of negotiation eligibility for products approved through an NDA [or BLA] is based on whether seven [eleven] years have passed since the NDA approval without reference to moiety [ingredient], reference product, or similar indicia of an intent to apply the term as broadly as set forth in the Initial Guidance.

We are also concerned that CMS' implementation creates a substantial set of burdens that were not envisioned when the IRA was enacted. For example, CMS' illustrative scenarios included one for which two manufacturers could be identified as a qualifying single-source drug. One of these manufacturers (the NDA/BLA holder) would be the primary manufacturer responsible for participating in the negotiation process, submitting complete and accurate information, and ensuring access to the maximum fair price (MFP). The primary manufacturer would be responsible for securing information that might be in the possession of, or even confidential to, the secondary manufacturer. The secondary manufacturer has no IRA-related obligations, yet its activities or

omissions could place the primary manufacturer in legal jeopardy in the form of substantial fines and penalties.

Manufacturers could not have foreseen the new landscape CMS' definition of a qualifying single source drug has created, and there may be no recourse available to primary manufacturers unable to comply with CMS' IRA requirements without information and other cooperation from secondary manufacturers. Neither the burden to primary manufacturers nor the substantial leverage that a secondary manufacturer might have in negotiating its compliance have been subjected to the notice and comment usually required when a significant burden is imposed on stakeholders. In fact, CMS did not acknowledge or discuss what, if any recourse it envisions would be available to primary manufacturers in its Initial Guidance.

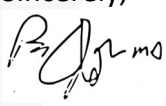
We urge CMS to reconsider its approach in advance of any legal challenges that might be asserted by manufacturers concerned that they have legal obligations with which they are logistically unable to comply. As noted above, we are concerned primarily with the uncertainty accompanying legal challenges to the implementation of laws designed to benefit patients. This is especially important if CMS' implementation of the new Part D out-of-pocket cost refinements is contingent upon moving forward with the IRA drug price negotiation program, and we ask that CMS inform the patient community that this is not the case.

Conclusion

Once again, we appreciate the opportunity to contribute the perspectives of those within the CLL/SLL patient and caregiver community as CMS implements the drug price negotiation provisions of the IRA. We strongly urge the Agency to expand the window for stakeholder feedback on this important and complex step toward drug selection and negotiation. The patient community has not had sufficient time to determine how the Initial Guidance changes incentives and disincentives, or whether it is more likely to benefit or harm patients. 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 feel free to contact me or Saira Sultan, CLL Society's Healthcare Advocacy & Policy Consultant, via email at saira.sultan@connect4strategies.com.

Sincerely,



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

CLL SOCIETY

VIA ELECTRONIC DELIVERY

June 20, 2023

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

RE: CMS-10849
Information Collection Request (ICR) for the Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act

Dear Administrator Brooks-LaSure:

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

CLL Society is dedicated to addressing the unmet needs of the chronic lymphocytic leukemia and small lymphocytic lymphoma (CLL/SLL) community through patient education, advocacy, support, and research. We are the largest nonprofit focused exclusively on the unmet needs of patients living with CLL and SLL.

Our patients live with a chronic, rare cancer of the immune system. We strive to fulfill our primary mission of ensuring that patients have access to safe and effective treatment options, which includes informing patients and caregivers about the therapeutic landscape. We also stress the importance of clinical trials to those in our community, build and support patient networks, engage in research, and educate patients and their caregivers.

CLL Society recognizes that the IRA's Medicare Drug Price Negotiation Program (DPNP) has the potential to significantly impact the reimbursement landscape, and consequently, the incentive framework driving (or in many cases deterring) innovation and investment for the foreseeable future. As we have noted in our comments to both CMS' Initial Guidance and its data elements ICR, we remain deeply concerned that any financial relief patients might experience from the DPNP will be far outweighed by its potential to exert a detrimental force on equitable access to existing treatments, and research and development toward new therapeutic options.

This ICR, unfortunately, compounds our concerns with the Initial Guidance and Data Elements ICR in that CMS has failed to acknowledge, much less incorporate, stakeholder comments that might

make the DPNP structurally viable while avoiding unintended consequences for patients living with CLL/SLL and other rare cancers. Our comments below provide a brief background on CLL/SLL and outline our overarching concerns with the framework that is articulated within CMS' Initial Guidance and carried over to the counteroffer process outlined in the ICR. We once again urge CMS to return to the collaborative approach that has historically resulted in well-reasoned processes that minimize unintended harm to beneficiaries.

Background

CLL/SLL is a chronic blood cancer of the white blood cells known as B-lymphocytes where there is a progressive accumulation of too many mature B-lymphocytes. CLL is the most common type of adult leukemia in the United States, with around 21,000 cases diagnosed annually. It is classified as both a type of leukemia and a type of non-Hodgkin's Lymphoma (NHL). SLL is simply a different manifestation of the same disease and is best understood as a stage of CLL where there are not yet a significant number of cancer cells located in the bloodstream. We, therefore, refer to the disease state collectively as CLL.

CLL is extremely heterogeneous, meaning each person's disease course and progression can vary considerably. Some patients have an aggressive form of the disease, experience rapid deterioration, and survive for as little as two years. Others have a less aggressive form of the disease, may never need treatment, and 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 and have transformed care for our patient community. Patients now have more treatment options compared to just years ago when the standard of care was chemoimmunotherapy. They can take continuous daily oral therapy with a BTK inhibitor (with or without the addition of a monoclonal antibody) until their disease progresses. Alternatively, patients can choose a short-term time-limited treatment approach that combines venetoclax and a monoclonal antibody. The latter approach allows for drug discontinuation until active monitoring reveals that another treatment is needed.

Although most CLL 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, and many are forced to either change treatments, take a "drug holiday," or adjust dosing due to drug intolerance. For patients with relapsed or 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 can experience serial relapses, and many will be treated with all available agents at some point during the course of their disease.

The experience with PI3K inhibitors in CLL illustrates the inherent difficulties associated with studying this disease and the heightened risk manufacturers must consider when pursuing new therapeutic candidates. Delays associated with the wait for overall survival data have already dampened research efforts and slowed patient access to potentially life-saving therapies. In addition, while we advocate for crossover in clinical trials to save lives, the strategy inherently compromises the "purity" of survival data. Therefore, CLL is not an ideal disease state from a research perspective. Historically, new treatments have been first approved for other cancers and then later approved for CLL.

DPNP implementation remains a high priority for CLL patients given the impact that it is already having on drug manufacturer and investor research and development decisions. CLL Society has received anecdotal reports of manufacturers retreating from pipeline projects, including those expanding FDA labels for existing treatments. In addition, a survey conducted on behalf of a trade association for the pharmaceutical industry confirmed that these reports may be indicative of a disturbing trend among drug manufacturers. A staggering three-quarters of manufacturer respondents indicated that they are reconsidering research strategies, and 78% said they will likely cancel early-stage pipeline projects due to uncertainties in DPNP implementation. Of particular importance to those with CLL, 95% of survey respondents stated that they expect to develop fewer follow-on indications for existing treatments (See https://catalyst.phrma.org/wtas-inflation-reduction-act-already-impacting-rd-decisions).

CLL Society continues to believe that CMS, with feedback from patients, providers, and industry stakeholders, has a pathway to implement the DPNP without disrupting incentives for innovation in CLL and other small population diseases. Each piece of the DPNP implementation that CMS has released, however, signals that the Agency either does not fully understand the impact of its policies or that it has determined to stay the course with those policies despite the impact. We have attached our written comments to CMS' Initial Guidance and its ICR on DPNP data elements and ask that CMS consider our concerns and recommendations as it moves toward selection of the first set of drugs that will be subject to price negotiation. Our comments on the counteroffer ICR are offered within the context of an overall framework that has yet to be fully outlined and vetted.

CMS' lack of transparency on the full negotiation process, including the initial offer and negotiation program agreement, hinders stakeholder efforts to submit meaningful feedback on the counteroffer ICR.

When CMS initiated its efforts toward implementing the DPNP, it provided stakeholders with assurances that it would solicit, consider, and incorporate stakeholder feedback into the DPNP processes. Although CMS has provided opportunities for stakeholder comment within the context of information collection activities, both the underlying paradigm of defining negotiation-eligible drugs by moiety or active ingredient (rather than New Drug Application [NDA] or Biologics License Application [BLA]) and the Primary/Secondary Manufacturer construct were devised without

affording patient communities an opportunity to comment. In addition, CMS has not followed up on identifying potential approaches to protect incentives for orphan drug research and development. CLL Society remains concerned that the opportunity to comment on the counteroffer ICR will have little real-world impact toward creating a viable DPNP that functions as Congress intended, unless CMS reconsiders the portions of the Initial Guidance released as "final."

With respect to the counteroffer ICR, we also note that:

- The breadth and extent of information CMS intends to present to both the public and the manufacturers with respect to the initial offer and its justification are crucial to determining whether the ICR is sufficient and less burdensome than alternative approaches.
    - CMS should provide stakeholders with an opportunity to comment on both the public and CMS-to-manufacturer information it expects to include in the initial offer and its justification.
    - CMS has not articulated how it will weigh feedback from the patient community on alternative treatment options and any added value associated with a particular drug.

- The ICR does not appear to contemplate a manufacturer response to feedback from other stakeholders. The following questions remain:
    - Will manufacturers be able to review the information submitted by patients and providers?
    - Will CMS provide an explanation on whether and how that information was incorporated into the initial offer?
    - How can manufacturers incorporate relevant information from the patient and provider communities into their counteroffer justification?

- The 1500-word limit on manufacturer submissions may be overly restrictive. We suggest that CMS work with manufacturers during the first year of DPNP implementation, and if necessary, later identify a limit that enables the submission of relevant information without overburdening CMS staff.

We would also ask that CMS provide greater transparency on the overall negotiation process so that stakeholders can contribute meaningful feedback on the counteroffer process and the sufficiency of CMS' ICR.

CLL Society is concerned that CMS has not resolved conflicts between its perspective on Primary Manufacturers and the real-world contractual arrangements that may constrain entities from submitting information and/or committing to a maximum fair price (MFP).

CLL SOCIETY

CLL Society has previously asked that CMS reconsider its determination to identify a qualifying single source drug based on common active moiety (drugs) or common active ingredient (biologics) (see attached). We reiterate our request that CMS treat products as the same qualifying single-source drug only when they share an NDA or BLA. This interpretation is within the plain language of the statute. Adhering to the plain language of the statute would not only reduce the burden to manufacturers seeking to comply with CMS' DPNP requirements, but it would also increase the nexus between the information collected and the true treatment value, including unmet needs addressed, and available alternative therapies.

We similarly reiterate our concern that CMS' implementation of a Primary/Secondary Manufacturer construct creates substantial sets of burdens that are not required under the statute. CMS' ICR asserts that the statute requires Primary Manufacturers **and only** Primary Manufacturers must submit all information related to the negotiation process, and agree to, reject, or propose a counteroffer in response to CMS' initial offer. Innovations in treating CLL and other rare cancers are often achieved through the efforts of small research-oriented entities that develop products through FDA submission and approval but rely on larger manufacturers for commercialization activities. Funds from licensing agreements or other arrangements are often invested in clinical studies toward new indications or the development of additional pipeline candidates. We expect the arrangements between a research and development entity and its commercialization partner(s) to take a variety of forms.

We strongly urge CMS to gain a clear understanding of whether (and how) existing agreements might interface with the IRA DPNP process, and potentially impede a CMS-identified Primary Manufacturer from full compliance. Additional questions remain, including the following:

- If a BLA holder is not responsible for commercialization activities, could contractual provisions prohibit that entity from accessing or disclosing information? Could contractual provisions also prohibit that entity from entering into pricing agreements with Medicare and/or other payers?

- Would a BLA holder without authority to negotiate drug pricing have liability for any excise taxes or other penalties that may arise from failure to submit information, propose a counteroffer, or agree on an MFP?

- What impact does the Primary/Secondary Manufacturer construct have on the value of drug products that are currently under development, and for which a commercialization and/or investment partner is needed?

- Would a BLA holder without the authority to agree to an MFP (or to cease sales related to federal payers) have any recourse for avoiding financial repercussions other than to withdraw its NDA/BLA for the product subject to negotiation?

CLL Society believes that having more robust stakeholder engagement would enable CMS to avoid situations in which a Primary Manufacturer would potentially face CMS-imposed penalties for contractual terms set prior to enactment of the IRA and its DPNP provisions. While we are unaware of whether NDA/BLA holders of the drugs that will be selected for the initial DPNP year will face any of the issues identified above, it is likely that CMS will encounter these issues (and, perhaps, others that we have not identified) in future years. CMS' estimates of the burden associated with the ICR do not appear to account for these scenarios.

Conclusion

CLL Society once again appreciates the opportunity to contribute the CLL patient perspective as CMS implements the DPNP. We remain hopeful that the Agency will take our comments and recommendations into account as it implements the DPNP, and we welcome the opportunity to discuss our comments and/or the experience of those living with CLL more generally.

If you have any questions, please feel free to contact Saira Sultan, CLL Society's Director of Government Affairs and Public Policy at ssultan@cllsociety.org.

Sincerely,

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

THE COALITION
FOR GOVERNMENT PROCUREMENT

Centers for Medicare & Medicaid Services
Office of Strategic Operations and Regulatory Affairs
Division of Regulations Development
Attention: Document Identifier/OMB Control Number: CMS–10849
Room C4–26–05
7500 Security Boulevard
Baltimore, MD 21244

Re: CMS–10849 Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)

Dear Mr. Parham:

The Coalition for Government Procurement ("the Coalition") appreciates the opportunity to respond to *Information Collection Request (ICR) for Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)*.

The Coalition is a non-profit association of over 350 Federal contractors, including leading pharmaceutical manufacturers potentially affected by Sections 11001 and 11002 of the IRA. Our member companies' portfolios cover healthcare, information technology, professional services and other industries and account for over $115 billion dollars in Federal contract obligations. For more than 40 years, the Coalition has promoted common sense in Federal procurement and best value solutions for Government, industry and American taxpayers.

Our comments on the ICR solely pertain to the proposed framework for Government and industry interactions in the price setting process outlined in the ICR. As proposed, the price setting process puts unnecessary limitations on the open dialogue and collaboration between Government and industry needed to establish maximum fair prices for covered drugs that meet the needs of Medicare patients, while minimizing unintended consequences for all patients and in the broader market.

Per the Supporting Statement accompanying the ICR, the price setting process begins after the submission of an initial Maximum Fair Price (MFP) offer from CMS to the Primary Manufacturer and is composed of the following steps:

> *(1) in accordance with section 1194(b)(2)(C) of the Act, an optional written counteroffer from the Primary Manufacturer (if CMS' written initial offer is not accepted by the Primary Manufacturer) that must be submitted no later than 30 days after the date of receipt of the written initial offer;*
> *(2) in accordance with Section 1194(b)(2)(D) of the Act, a written response from CMS to the optional written counteroffer;*
> *(3) if the Primary Manufacturer's written counteroffer is not accepted by CMS, up to three possible in-person or virtual negotiation meetings between the Primary Manufacturer and CMS;*
> *(4) a final written offer made by CMS to the Primary Manufacturer; and*

(5) a response by the Primary Manufacturer to CMS' final written offer, either accepting or rejecting this final offer.

Proposed CMS guidance[1] from March clarifies that in the third step, CMS intends to hold at least one in-person or virtual negotiation meeting with the manufacturer prior to a final written offer. The manufacturer and CMS then may each request one more negotiation meeting, but they are limited during negotiations to a total of three meetings. The guidance does not require or suggest meetings between manufacturers and CMS at any other point in the drug selection, initial offer development, and price setting process.

The Coalition recognizes the opportunity for CMS and industry to meet in the third stage of the process to allow both parties to exchange information about each other's offers and the benefits and risks of any potential agreement. We are concerned, however, that placing a cap on the number of meetings could impose an artificial constraint, and we believe that the Drug Price Negotiation Program could benefit from guidance that promotes greater communication and collaboration between the Government and manufacturers.

Therefore, we recommend that CMS revise the proposed price setting process for the Drug Price Negotiation Program to ensure that CMS representatives and industry can engage in constructive dialogue, to include sharing CMS's evaluation and interpretation of industry's input. CMS and industry should be encouraged to engage in open communications in the best interest of patients and innovation, without arbitrary limits (e.g., the number of meetings and the length of dossier submissions) established through regulation.

The Federal Procurement System Provides a Model for How CMS can Engage with Industry

Congress, Federal regulators, and acquisition officials have long recognized the value of open communication between Government and industry in driving best value pricing and solutions for American taxpayers in the Federal procurement system, which purchased over $1.1 trillion dollars of goods and services in FY 2022. Open dialogue between Government and industry in the pre-solicitation process is encouraged by the Federal Acquisition Regulation (FAR) and in guidance from the Office of Management and Budget (OMB). Contract programs within the U.S. Department of Veterans Affairs, the Defense Health Agency, and the Defense Logistics Agency that procure and negotiate prices for pharmaceuticals for millions of military service members and their beneficiaries, provide opportunities for industry to meet and engage with the Government throughout the acquisition process.

The Medicare Drug Price Negotiation Program is not an acquisition program, though it requires industry and Government to agree on prices subject to a set of terms and conditions. Therefore, it stands to reason that there may be best practices for the negotiation of drug pricing under Federal contracts that are also pertinent to CMS's price setting. Guidance on Government and industry communication from the FAR and OMB suggests that CMS and manufacturers should engage in an open dialogue throughout

[1] Center for Medicare and 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, https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf.

the entire process from selection to price setting, that CMS should be open to meeting requests, and remove artificial caps on the number of meetings and types of engagement.

The FAR is the primary regulation used by Executive agencies in the procurement of products and solutions and ensures that all procurement procedures are standard and conducted in a fair and impartial manner. In Part 15[2] of the FAR, "Contracting by Negotiation," contracting officers are encouraged to participate in pre-proposal discussions and post-proposal negotiations with industry. There is no specific mandate in the FAR that limits the number of times a contracting officer can meet with industry during negotiations.

In addition to Part 15, FAR Part 1 was amended in December 2022 to emphasize the importance of effective communication between Government and industry in the negotiation of Federal contracts in accordance with Section 887 of the National Defense Authorization Act (NDAA) for FY 2016. Per FAR Part 1.102-2 (a)(4):

> *The Government must not hesitate to communicate with industry as early as possible in the acquisition cycle to help the Government determine the capabilities available in the marketplace. Government acquisition personnel are permitted and encouraged to engage in responsible and constructive exchanges with industry (e.g., see 10.002 and 15.201), so long as those exchanges are consistent with existing laws and regulations, and do not promote an unfair competitive advantage to particular firms.*

In the spirit of the FAR Part 1 and 15, we recommend that CMS encourage responsible and constructive informal exchanges between CMS and manufacturers, early in the price setting process and often, while doing so consistent with law and regulation and in a manner that does not promote unfair competitive advantage.

Further, in its series of governmentwide memoranda refuting "myths" in Federal contracting, beginning with the "*'Myth-Busting": Addressing Misconceptions to Improve Communication with Industry during the Acquisition Process*" memo in February 2011, OMB emphasized that having access to current market information is critical to the Government as they define contract requirements and negotiate associated terms and conditions. OMB also recognized that:

> *"our industry partners are often the best source of this information, so productive interactions between federal agencies and our industry partners should be encouraged to ensure that the Government clearly understands the marketplace and can award a contract or order for an effective solution at a reasonable price."*

Arbitrary limits on Government and industry communications in the price setting process run contrary to the spirit of FAR and OMB guidance. They risk depriving the Government of important information about the risks and benefits of prices set, and the potential impacts on areas beyond each individual agreement that are critical to *all* patients, like clinical research and innovation.

[2] FAR Part 15.201 Exchanges with industry before receipt of proposals, https://www.acquisition.gov/far/part-15#FAR_15_201

Recommendations

In short, the Coalition recommends that CMS revise the proposed price setting process for the Drug Price Negotiation Program to:

1. Ensure that CMS representatives and industry have an opportunity to engage in constructive dialogue, without arbitrary or artificial limitations to such dialogue, during the price setting process, so that meaningful information sharing occurs between CMS and industry partners, including but not limited to CMS's evaluation and interpretation of industry's input.
2. Focus on achieving the maximum price for negotiated drugs, in the best interest of patients so as to not jeopardize access to innovation, as the desired outcome of the price setting process (versus meeting certain requirements on the number, type and scope of industry communications).
3. Eliminate arbitrary limits on achieving this objective, including limitations on the number of meetings and limits to the length of dossier submissions.

We believe that these revisions to the price setting process will help to ensure that Medicare beneficiaries continue to receive access to covered drugs and that all patients continue to benefit from the pharmaceutical industry's investments in critical drug research and innovation.

Thank you for considering industry's comments in response to the Drug Pricing Negotiation Counteroffer Information Collection request. If you have any questions, please contact Roger Waldron at rwaldron@thecgp.org or (202) 331-0975.

Sincerely,

Roger Waldron
President

GSK Comment Letter

Response to Information Collection Request for Negotiation Supporting Statement – Part A, and Counteroffer Form

June 20, 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 Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849, 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 for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (ICR or the ICR), including the Federal Register Notice, Supporting Statement – Part A, and the ICR Form (Counteroffer Form) (CMS-10849, 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 medicines, and general medicines. Our global specialist HIV company, ViiV Healthcare, is fully dedicated to delivering advances in prevention, treatment, and care for people with HIV.

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

GSK urges CMS to eliminate the Primary/Secondary manufacturer construct given the complexities it adds 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 the necessary information applicable to any Secondary Manufacturer(s).[1] 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

[1] 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.

Primary Manufacturer to collect, report, and certify the accuracy and correctness of the Secondary manufacturers' data is not possible because the Primary Manufacturer does not have access to other manufacturer data, cannot compel the Secondary Manufacturer to provide the data, and would have no way to ensure another manufacturer's data are accurate.

Additionally, manufacturers may not want to disclose confidential and/or proprietary information to another manufacturer. Any existing contractual arrangement between manufacturers does not conceive of a Primary/Secondary manufacturer framework nor does it include provisions requiring a Secondary manufacturer to share information accurately and completely. Under the proposed guidance, a Primary manufacturer must certify completeness without considering the current contracts among certain manufacturers. Therefore, CMS should require the Primary and the Secondary Manufacturer to separately submit and 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, which is an unjust penalty when Primary Manufacturers have no ability to verify the data and attest to its veracity should it even be available. 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 anti-trust laws if it collects pricing information from a Secondary Manufacturer. The counteroffer process creates additional burden on Primary manufacturers to provide more proprietary and/or confidential information. In its final Medicare negotiation guidance and for the counteroffer process, CMS should abandon the Primary / Secondary Manufacturer framework due to the added complexities and burden of data collection that the framework creates.

CMS should develop a process for more meaningful manufacturer engagement that begins as early as possible

CMS proposes to allow up to three potential meetings with a manufacturer as part of the Maximum Fair Price (MFP) decision-making process but only at the end of the process in instances where a manufacturer's written counteroffer is not accepted by CMS. GSK is concerned that this proposal timeline to meet with manufacturers is too late in the process. Open communication between a manufacturer and CMS is an essential step before the counteroffer process and will be particularly important given the broad range and disparate types of data (from manufacturers and public stakeholders) and assumptions that will factor into MFP determination. We remind CMS the unique position of manufacturers as being experts on their medicines. Therefore, GSK urges CMS to revise its process to allow earlier, more meaningful manufacturer engagement to include meetings before the counteroffer stage of the process. We recommend allowing manufacturers to engage with CMS upon publication and inclusion on the list of selected drugs for negotiations.

Further, CMS should provide a thorough and comprehensive explanation for the initial price offer. The rationale should describe how the manufacturer submitted data and the factors considered by CMS factors into the initial offer, including the justification for selected therapeutic alternatives and how the various factors were weighed. Manufacturers require this information to produce a substantive and meaningful counteroffer.

CMS should foster flexibility with manufacturer submission by eliminating word limits

Given the extensive amount of data that CMS is requesting from manufacturers, and the requirement for manufacturers to provide a justification for a counteroffer based on these factors, CMS can foster flexibility in manufacturer submission by removing word limits. A response limited to 1,500 words (which is equivalent to 2.5 pages) will not allow for a meaningful response that covers the essential elements and explanations that are to be considered in the process. Any word limit is contrary to the statutory requirement for manufacturers to provide complete information. A 1,500-word limit would invariably result in manufacturers omitting vital information. The current word limit is insufficient to explain manufacturer assumptions, rationales, and approaches used, and may lead manufacturers to cherry pick data and eliminate key details to meet this word limit requirement.

GSK also encourages CMS to provide space for manufacturers to attach key information sources that support the manufacturer's counteroffer response. While GSK appreciates that CMS is seeking to contain submissions so as not to strain agency resources in reviewing these materials, allowing for additional content and explanation will give rise to greater understanding, better decision making, and potentially eliminate the need for unnecessary back and forth communication to clarify submissions.

CMS should modify the certification requirement

As mentioned in GSK's comments on the Negotiation Data Elements ICR, CMS 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. In addition, CMS should remove the liability clause(s) from the certification process to align with other similar processes. CMS should adopt a similar policy as certifying Average Sales Price Data submission where manufacturers must certify without any liabilities that the information submitted is in accordance with submitter's best "knowledge and belief" and "made in good faith." CMS is currently seeking an extensive set of data while simultaneously limiting the number of words that can be entered as a response. Thus, CMS' proposed word limits run counter to certifying completeness of manufacturer data.

GSK appreciates the opportunity to provide comments on the Negotiation Process 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: CMS-10849
Information Collection Request (ICR) for the Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act

Dear Administrator Brooks-LaSure:

Haystack Project appreciates the opportunity to provide comments on the Centers for Medicare & Medicaid Services' (CMS') Information Collection Request (ICR) in connection with the manufacturer counteroffer process under the Inflation Reduction Act's (IRA's) Drug Price Negotiation Program (DPNP).

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 disease states where unmet need is high and treatment delays and inadequacies can be catastrophic.

Since its inception, Haystack Project has engaged with CMS through comments on CMMI model proposals, implementation and refinement of the Medicare Quality Payment Program (QPP) and the Affordable Care Act, as well as throughout annual rulemaking cycles refining policies under Medicare Parts A, B, C and D.

Since enactment of the IRA, Haystack Project membership has continued to grow – both in numbers (nearly doubling to over 140 ultra-rare disease advocacy organizations) and in the collective concern that the drug price negotiation program could threaten the fragile balance

that has historically enabled an adequate return on investment for targeted treatments in small population diseases and rare cancers.

Our community of patients and caregivers were initially hopeful that CMS would implement the drug price negotiation program with proactive and intentional consideration of the complex set of incentives and risks associated with developing treatments in the ultra-rare disease space. Our comments (attached) to CMS' Initial Guidance implementing the DPNP articulated our concerns with CMS' approach. Haystack Project restated those concerns within the context of the negotiation data elements ICR, asserting that the sufficiency of the data elements within the ICR and the burden associated with providing that information were inextricably linked to and vastly impacted by the Initial Guidance. Unfortunately, each piece of the process CMS releases has revealed the Agency's adherence to an approach that will unnecessarily, and potentially inextricably, tip the scales away from innovation.

Haystack Project believes it is not only possible, but imperative, that CMS implement the DPNP to align with our shared goal of ensuring that Medicare drug prices reflect treatment value ***without*** disrupting incentives toward innovation in rare disease therapies. We reiterate our recommendations that CMS:

- Reconsider its decision to define qualifying single source drug based on moiety or active ingredient rather than NDA/BLA.

- Replace the Primary/Secondary Manufacturer framework with a more flexible approach that can be adapted to the contours of contractual arrangements when there is more than one manufacturer for a selected drug.

We also provide our comments, concerns, and recommendations specific to the counteroffer process and urge CMS to be more transparent and collaborative with respect to the negotiation process as a whole. Unfortunately, stakeholder input on the counteroffer process is substantially compromised by the fact that the processes leading to and following this phase of negotiation are unknown to the public.

Background: Individuals with Rare and Ultra-Rare Conditions and Rare Cancers will be Disproportionately Impacted by the IRA's Potential to Deter Innovation.

Although countless lives have been improved or saved by new therapies enabled by Congress' set of incentives for orphan drugs, significant unmet need predominates in extremely rare conditions and rare cancers:

- Of the approximately 7,000 rare diseases identified to date, 95% have no FDA-approved treatment option.
- 80% of rare diseases are genetic in origin, and present throughout a person's life, even if symptoms are not immediately apparent.

- Diagnosing a patient with a rare disorder is usually a multi-year process involving a series of primary care clinicians, specialists, and diagnostic testing regimens – extreme rarity of a disorder compounds the resources required for diagnosis.
    - Patients often progress to more serious and more costly disease states by the time they receive a diagnosis.
- If a diagnosed condition has no FDA-approved option, treatment often involves off-label use of existing products.
- Approximately half of identified rare diseases do not have a disease-specific advocacy network or organization supporting research and development, and lack of disease-specific natural history severely complicates research toward new, targeted treatments.

Patients suffering from rare diseases that are currently untreatable have maintained hope that the incentives toward innovation, coupled with increased scientific understanding of disease mechanisms, would stimulate progress toward treatment and, eventually, a cure. For patient populations approaching the 200,000 orphan disease limit, current incentives have proven to be sufficiently robust to mitigate clinical trial and reimbursement risks. As affected populations dwindle below 20,000 or even into and below the hundreds, the balance can be far more tenuous, and risks or uncertainties can discourage the investor interest required to take promising therapeutic candidates from bench to market. The DPNP has the potential to place an abbreviated timeline for recouping return on investment into the already-complex risk/benefit analysis for ultra-rare disease treatments.

Haystack Project urges CMS to reconsider its decision to identify negotiation-eligible drugs based on moiety or active ingredient rather than NDA/BLA.

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.

- 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.

    - CMS has not indicated how it would assess information on multiple NDAs that include one or more orphan indications. Would value in small population indications have a greater or lesser impact on CMS' initial offer compared to uses in more common diseases?

    - It is also unclear whether CMS would subject a subsequently-approved orphan indication to the maximum fair price (MFP).

        - The negotiation data elements ICR indicated that CMS would not take into account any research and development costs associated with indications that had not yet been approved. It is unclear whether CMS would accept this information within the counteroffer process.

        - CMS' definition of qualifying single source drug could increase pressures on manufacturers to sell follow-on NDAs/BLAs and exact artificial negative pressures on the value of those asset(s) that ultimately deter innovation in ultra-rare diseases.

CMS has yet to respond to our concerns that CMS' definition went beyond the type of simple implementation of statutory requirements Congress envisioned the Agency completing without notice and comment. We remain concerned that CMS made a policy decision, and that policy decision has driven a statutory interpretation beyond and in likely conflict with the plain language of the IRA.

- 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.

        - 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.

        - Stakeholders cannot contribute meaningful feedback to the counteroffer ICR without further guidance on how CMS would identify a single MFP across NDAs/BLAs in diverse indications with variable unmet needs and no single alternative treatment optioin

- 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 is innacurate and arbitrary if applied equally to indications with and without alternative treatment options.

CMS' Primary/Secondary Manufacturer structures are particularly problematic within the context of 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.

The counteroffer process introduces additional wrinkles that CMS may not have considered. The overarching lack of transparency into the entirety of the negotiation process makes it impossible to determine how CMS will accommodate situations in which the BLA holder has contractual arrangements that preclude it from agreeing to an MFP, proposing a counteroffer, or rejecting CMS' initial offer. We strongly urge CMS to engage industry stakeholders to pressure-test the assumption that all NDA/BLA holders will have (1) access to all information CMS needs within the DPNP process; (2) authority to disclose all required information; and (3) authority to agree to or reject an initial offer or propose a counteroffer applicable to all NDAs/BLAs within CMS' definition of a qualifying single source drug selected for negotation.

Haystack Project believes that the most prudent approach would be for CMS to refine its definition of a qualifying single source drug and implement a more flexible mechanism for

obtaining negotiation-relevant information and securing agreement on an MFP. Put simply, the burden associated with providing information a manufacturer has no legal recourse to access, much less disclose, and penalizing entities for failing to act on drug pricing agreements they are contractually prohibited from entering into is both enormous and avoidable.

The information currently available on the negotiation process does not illuminate how non-manufacturer stakeholder input will be incorporated into the initial offer or the counteroffer process.

The negotiation data elements ICR provided for public input into the consideration of alternative therapeutic options. We previously expressed our concerns that the process for submission, limitation of information content and quantity, and certification requirement will substantially deter input from patient advocacy organizations. Haystack Project reiterates those concerns and further urges CMS to outline how input from patients and providers will be incorproated into the initial offer, as well as the extent to which manufacturers will have access to that information as they propose a counteroffer.

In addition, off-label uses in ultra-rare conditions may not be factored into CMS' initial offer. Permitting manufacturers to submit information on unmet needs and other relevant information within the counteroffer process is an important step toward underscoring the relevance of our patient communities to manufacturers and the Medicare program.

- 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 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 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 not be able to identify condition-specific options or state that there are no alternative therapies.

The Orphan Drug Exclusion Should be Implemented to Maintain Incentives for Developing New Treatments in Rare Conditions and Expanding Labeled Indications of Existing Therapies

Haystack Project appreciates that CMS recognizes the need to protect access to orphan drugs currently available as well as innovations that have yet to be developed. We fully support CMS' determination to qualify drugs for the exclusion based on whether approved indications are within a single designation. Unfortunately, the policy on defining a qualifying single source drug by active moiety/ingredient discussed above will likely reduce manufacturer interest in pursuing multiple indications within or beyond a single designation.

The initial year(s) for the DPNP will likely shape investory perspectives on the value of pursuing new treatments for ultra-rare diseases and/or seeking FDA approval for new ultra-rare uses of existing drugs. It is, therefore, imperative that CMS take steps toward protecting the incentives currently in place for rare disease product development. Patients with ultra-rare conditions and rare cancers are particularly concerned that:

- Manufacturers will face pressures to focus on an orphan indication with the largest patient population.

- Research and development programs confirming clinical benefit for accelerated approval treatments may be halted and indications withdrawn if those indications fall outside a single orphan drug designation.

- Pressures to focus on larger-population orphan designations/indications could delay product approval and increase initial research and development costs.

- The IRA's chilling effect on research and development will fall disproportionately on patients with ultra-rare diseases and rare cancers.

- Investors and shareholders will seek to ensure that initial price points for newly-approved drugs are sufficient to recoup research and development costs and achieve a profit margin from successful innovations.

Once again, we appreciate that CMS has limited discretion in implementing the orphan drug exclusion. In its Initial Guidance, CMS sought stakeholder feedback on how it might implement the IRA drug price negotiation program without detering access and innovation in rare diseases. We urge CMS to take concrete steps to preserve viability of orphan indications with particular atttention to the unique circumstances within the ultra-rare disease communities, including that it:

- Work with patient and industry stakeholders to remove the single orphan designation requirement from the IRA orphan drug exception.

- Identify qualifying single source drugs by NDA/BLA (as more fully outlined in the preceding sections).

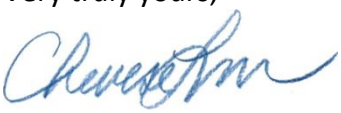
- Engage in meaningful dialogue with Haystack Project and other patient-centered ultra-rare disease organizations to preserve the balance in incentives and risks that has spurred innovation in rare and ultra-rare disease treatments, including through CMMI and CMS' general demonstration authority.

- Implement a transparent process for manufacturers to submit evidence demonstrating that a particular product is eligible for the orphan drug exclusion.

Conclusion

Haystack Project appreciates the opportunity to submit feedback on the counteroffer ICR. 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,



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June 20, 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–10849 Information Collection Request for Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)

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–10849 Information Collection Request for Drug Price Negotiation Process 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.

The Inflation Reduction Act (IRA or the Act) creates a new price-setting mechanism that will change the economic incentives for bringing new medicines to market and investing in ongoing post-approval research and development. 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] We understand that CMS has a statutory requirement to implement the IRA, incorrectly portrayed as "negotiation," as it forces manufacturers to accept CMS's final price, face an unreasonable excise tax, or exit the market. In implementing the Act, CMS should seek to establish a process that accurately values

[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

medicines and maintains patient access, two goals that necessitate robust and iterative stakeholder engagement.

NPC appreciated the opportunities 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) as well as the Data Negotiation Element ICR for CMS's Drug Price Negotiation Program. We further appreciate the opportunity to comment on this Drug Price Negotiation Process ICR. NPC encourages CMS to structure its initial written offer and the counteroffer form in ways that promote transparent exchange and evaluation of evidence on the value and clinical benefit of selected drugs. Specifically, we recommend that CMS:

1. Establish a transparent, replicable structure for CMS's initial written offer.
2. Provide opportunities for in-person CMS-manufacturer engagement before manufacturers' submission of their written counteroffers.
3. Remove inappropriate constraints while acknowledging response burden.

Establish a transparent, replicable structure for CMS's initial written offer.

This counteroffer form, even in combination with the Guidance, provides no meaningful insight into how CMS will evaluate drugs or the factors considered during the price-setting process. The instructions for the counteroffer form state that manufacturers should provide a justification of the counteroffer, based on the factors in section 1194(e) of the Act, that responds to the justification provided in CMS's written initial offer. However, no details on the structure or content of CMS's offer have been communicated. More robust transparency surrounding CMS's drug evaluation process, evidentiary standards, and the format of the initial offer would not only align with fundamental government transparency and best practices for comparative effectiveness research but would also facilitate more efficient and productive communication between manufacturers and the Agency. The need for transparency is further underscored by the statutory requirement that the written counteroffer be submitted within 30 days of receiving the written initial offer from CMS, which constrains flexibility and CMS-manufacturer discussions following the initial offer.

We encourage CMS to promote transparency by publishing its evaluation framework and the structure of the initial offer before beginning the evaluation process. The Instructions for Completing the Counteroffer Form indicate that manufacturers should respond to the justification provided in CMS's initial offer and provide the reasons the manufacturer believes information related to the selected drug and its therapeutic alternatives do not support the written offer. In order to do so, manufacturers must be given a clear and comprehensive rationale for the initial offer price, including the Agency's evaluation of evidence submitted by diverse stakeholders. Specifically, we recommend that CMS include a number of data elements in the initial evaluation framework with specific details in its initial offer:

1) the therapeutic alternative(s) considered for each indication for selected drugs and the rationale for selection;

2) the application of the definition of unmet need to each indication of selected drugs;
3) the full range of benefits and impacts considered for each indication;
4) the internal process and rationale for determining which benefits and impacts were considered;
5) a list of each stakeholder consulted;
6) the source(s) of evidence considered, particularly of patient, clinicians and any de novo analyses conducted by CMS;
7) how each benefit and impact considered influenced the final MFP, to include any algorithms, calculations, or modeling that related to MFP determination, as well as rationale for evidence that was not considered; and
8) the Agency's evaluation of the quality of submitted evidence based on accepted rubrics for evaluating study quality;
9) the limitations of the data collected and uncertainties in CMS's decision-making.

In addition, CMS outlined in its Guidance an initial process for setting a single price across all dosage forms and strengths using an average price per 30-day equivalent supply for the selected drug. The use of loading doses, weight-based dosing, and severity-based dosing are common clinical practices that result in the amount of medicine being used by one patient being different than that used by others. These complexities of calculating a 30-day equivalent supply emphasize the need for further clarity on CMS's process as well as ongoing and open communication with manufacturers. We further recommend that CMS provide in its initial offer detailed explanations of its calculation of 30-day equivalent supplies, including how its weighting and assumptions compare with actual use across the Medicare population. This information will be vital for manufacturers of selected drugs with variable dosing to formulate a responsive counteroffer.

Provide opportunities for in-person CMS-manufacturer engagement before manufacturers' submission of their written counteroffers.

NPC encourages CMS to implement a transparent and inclusive evaluation process to improve credibility and support for their price-setting and counteroffer process. Robust engagement with manufacturers is critical to establishing credibility and is consistent with the practices and policies of other payers and regulators. The ICR Form, along with CMS's initial Guidance, states that up to three in-person or virtual negotiation meetings will be possible "if the written counteroffer is not accepted by CMS." This approach limits the opportunity for manufacturers to meaningfully inform and participate in the "negotiation" process, which is complicated by an inflexible negotiation data elements form with arbitrary word counts and as discussed below, an unjustifiably constrained counteroffer form. These restrictions run counter to established

principles for drug evaluation, which encourage active engagement of all key stakeholders in all stages of an evaluation process.[2]

We urge CMS to engage manufacturers at additional points during the MFP process beyond those specified in the initial Guidance and counteroffer ICR, including *at a minimum,* in-person meetings: (1) after drug selection, and (2) prior to CMS presenting the initial offer. The latter of these meetings would provide opportunities for CMS to discuss the initial offer and its rationale with manufacturers before the start of the 30-day submission deadline for a counteroffer. In-person meetings to discuss CMS's rationale for their initial offer will improve transparency and reduce manufacturers' burden of responding to the initial offer within the short time frame established by the statute.

Remove inappropriate constraints while acknowledging response burden.

In its implementation of the IRA, NPC urges CMS to promote a collaborative approach to information exchange that allows stakeholders, including manufacturers, opportunities to provide comprehensive evidence on drug value. The ability of stakeholders to communicate relevant information should not be constrained by arbitrary and limited word counts. Answers to Question 3 on the initial counteroffer form are limited to 1500 words. In those 1500 words, manufacturers are expected to: respond to the justification provided in CMS's initial offer; provide the reasons the manufacturer believes information submitted by the primary manufacturer and other available data related to the selected drug and its therapeutic alternatives do not support the written offer; and provide justification of their counteroffer based on the factors in section 1194(e) of the Act. The arbitrary word limit imposed on the manufacturer's counteroffer unjustifiably constrains their ability to meaningfully engage with CMS in scientific dialogue on the evidence evaluation and inform CMS's decision-making surrounding their counteroffer. We urge CMS to eliminate restrictive word counts for information collection responses.

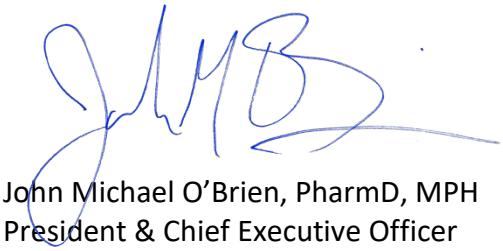
The counteroffer form states that the time required to complete this ICR is estimated to average 79 hours per response, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. An informed response to an initial offer that both responds to the initial offer and provides robust justification for a counteroffer necessitates far more than 79 hours. We encourage CMS to reduce the burden associated with the counteroffer by establishing a robust, replicable evaluation framework and transparently communicating – through 2 pre-offer meetings, the initial offer letter, and any additional in-person meetings – its application of the framework to a price determination. Doing so would improve transparency and reduce manufacturers' burden of writing counteroffer responses to include relevant information for CMS's evaluation.

[2] Drummond M, Schwartz JS, Jansson B, Luce BR, Neumann BR, Seibert U, Sullivan SD. Principle 10. Key Principles for the Improved Conduct of Health Technology Assessments for Resource Allocation Decisions. International Journal of Technology Assessment in Health Care. 2008. 24:3:250.

Conclusion

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

June 20, 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

RE: CMS-10849

Dear Administrator Brooks-LaSure,

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) for the counteroffer component of the draft guidance '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,' hereafter referred to as the "Negotiation Program" guidance.

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.

NORD appreciates CMS' willingness in the Negotiation Program guidance (Section 30.1.1) to consider additional actions to "best support orphan drug development" and is pleased to submit the following comments to help CMS make good on its commitment to the rare disease community.[1] These comments are intended to supplement the April 14th comment letter submitted by NORD. As discussed in NORD's April 14th comments (linked here), successful implementation of the Negotiation Program hinges on CMS:

1. Ensuring rare disease patients have meaningful opportunities to submit patient experience data and provide valuable insights given the unique value of the negotiated products to rare disease patients, and the scarcity of published data specific to rare diseases;

[1] Meena Seshamani, Memorandum to Interested Parties: 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, at 10- 11.

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2. Ensuring rare disease patients have access to the negotiated therapies through appropriate formulary placement and limited or no utilization management barriers;
3. Further clarity around the implementation of the orphan drug exclusion to ensure orphan products remain excluded from negotiation until the product is FDA-approved for a second disease; and
4. Tracking the impact of IRA implementation immediately.

NORD thanks the agency for recognizing, in Section 60 of the draft guidance, the value that orphan drugs can provide to specific parts of a negotiated product's patient population.[2] NORD also appreciates CMS' objective to assess value in an indication specific manner, allowing the full range of patient values for a product to be captured. However, as outlined in our April 14th comments, NORD is concerned that CMS' proposed approach to the Negotiation Program would not allow patients to submit patient experience data, including missing, but critical, information on patient perspectives regarding unmet needs, clinical benefit, and therapeutic alternatives, in a meaningful manner.
Specific to the counteroffer process, NORD urges CMS to ensure rare disease patient perspectives are appropriately considered in the process by:

a. **Ensuring CMS has access to the relevant, high quality patient experience data as the agency is crafting the initial offer and during every step of the negotiation process; this means ensuring that the data submission process works for the impacted patient communities, proactively collecting patient experience data as needed, and allowing for meaningful patient comments during every step of the negotiation process. Specifically, we urge CMS to:**

- Make it easier for patients to participate in the data submission process. Increased accessibility measures could include interfacing with leaders of the appropriate disease specific community, accommodations for individuals with impairments, and clear instructions with applicability criteria to ensure information is being appropriately and adequately sourced.

- Clarify the information the agency is seeking from patients and the timeline on which the Agency seeks to receive such information to ensure a rigorous, standardized approach to data collection. Given the short timelines for collecting data prior to negotiations, the submission process and expectations should be clarified well in advance so that community leaders may have time to appropriately aggregate patient stories and respond in a meaningful manner.

- Use the FDA's experience with patient listening sessions to organize similar meetings to inform patient voice discussions on negotiated drugs. For example, FDA's Voice of the Patient reports help to capture the patient perspective of a drug by soliciting information about therapeutic alternatives, unmet need, and clinical benefit of alternatives. Patient submissions lacking standardization run the risk of becoming a series of anecdotes, rather than concrete and actionable information. NORD recommends utilizing FDA's "Patient Focused Drug Development: Collecting Comprehensive and Representative Input" guidance

[2] Meena Seshamani, Memorandum to Interested Parties: 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, at 10- 11.

as a framework for successful data collection and management practices. By increasing the standardization of submissions, the agency will ensure that patient time spent responding to the comprehensive data submission will be useful in informing the initial offer and counteroffer process for products selected for negotiation.

- Additional submission periods during the negotiation process could also increase the opportunity for the community to submit valuable information. To ensure patient input is given the due consideration it deserves, NORD recommends extending public comment periods and allowing patients to submit additional information during the counteroffer process. As the submission process is voluntary, and not subject to the statutory data submission timeline and contents for manufacturer provided data, CMS should work with the patient community to determine timelines that would be feasible to submit relevant supporting information for both the initial offer and counteroffer processes.

- Furthermore, allowing patient stakeholder comments at subsequent steps of the submission process including during the counteroffer process will allow the patient community to react to CMS' initial proposal and provide supplemental data as appropriate.

b. **Establish a process for engaging the patient community in the counteroffer process.** CMS' proposed approach does not include the patient community in the counteroffer progress at all and, in fact, severely restricts what information manufacturers are allowed to share about the negotiation process, making it almost impossible for the patient community to meaningfully contribute to the counteroffer process. NORD strongly urges CMS to engage patients in the counteroffer process. For instance, patients can, under certain circumstances, join confidential meetings between the Food and Drug Administration and drug sponsors to provide critical insights on patient perspectives during these regulatory meetings. In fact, countless drug development programs have benefited from the inclusion of patients at critical junctures of the regulatory interactions, and NORD urges CMS to work with FDA, patient groups, and manufacturers to develop an analogous process for the counteroffer process.

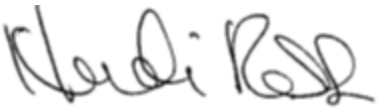
c. **During the negotiation process, clearly and transparently communicate to manufacturers and other key stakeholders how patient experience data was incorporated in developing the initial and subsequent offers.** To support robust, meaningful patient engagement, and to ensure relevant orphan-indication specific data is being used to support the Negotiation Program from the initial offers throughout the negotiation process, NORD recommends all initial and subsequent offers include a detailed outline of the data sources utilized to establish an initial offer including where and how patient experience data was used to arrive at the initial (and subsequent) offer. NORD recognizes that initial (and subsequent) offers may be kept confidential. However, transparency for everyone privy to the offer on the factors and decisions made in establishing an initial offer and counteroffer(s)will allow patients to meaningfully provide insights on specific community perspectives to the negotiation process and increase the efficiency and effectiveness of the negotiation process.

d. **Upon completion of the negotiation process, CMS should provide public, granular summaries of the data and assumptions on which the final offer or negotiated price was**

based, including what patient experience data was used and how; this will help create consistency and trust in the negotiation process. A negotiation process lacking specific and granular summaries of patient value and data sources utilized could be perceived as lacking validity. Additionally, processes to establish patient-specific input and data standardization will allow CMS to specifically articulate the value that negotiated drugs have to the patient community.

We again thank CMS 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. For questions related to this letter, please contact Heidi Ross, Vice President of Policy and Regulatory Affairs (HRoss@rarediseases.org) or Karin Hoelzer, Director of Policy and Regulatory Affairs (KHoelzer@rarediseases.org).

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

June 20, 2023

Submitted via
Electronic Filing: https://www.regulations.gov/document/CMS-2023-0064-0001

Centers for Medicare & Medicaid Services
Office of Strategic Operations and Regulatory Affairs
Division of Regulations Development
Attention: Document Identifier/OMB Control Number: CMS-10849, OMB, 0938-NEW
Room C4–26–05
7500 Security Boulevard
Baltimore, MD 21244–1850

RE: Novo Nordisk Comments on *CMS-10849 Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)*

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 *Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA).*

Novo Nordisk is a global health care company committed to improving the lives of those living with serious chronic conditions, including diabetes, hemophilia, growth disorders, and obesity. The Novo Nordisk Foundation, our majority stakeholder, is among the top five largest charitable foundations in the world. 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.

The Medicare Drug Price Negotiation Program, outlined in the IRA and described in recent guidance, represents an unprecedented and fundamental shift in the way that prescription drugs are developed, valued, distributed, and sold. Though the Agency has released draft implementation guidance and multiple ICRs to date, the Agency's proposed approach has only increased the uncertainties introduced by the IRA's new Drug Price Negotiation Program and underscored the need for more public input, for a more deliberate process, and for additional communication channels with the Agency. Novo Nordisk is concerned that, despite assurances that the Agency "intends to prioritize transparency and robust engagement among all interested parties,"[1]the process outlined for negotiation, including the submission of a counteroffer using the form described in this ICR, deprives manufacturers of opportunities to provide meaningful input and cannot be described as a true, reciprocal "negotiation."

[1] https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf

Novo Nordisk offers the following comments to address certain flaws in CMS's proposed approach. As a member of the Pharmaceutical Research and Manufacturers of America ("PhRMA"), we also support the comments submitted by PhRMA in response to CMS's ICR.

CMS should abandon the concepts of "Primary Manufacturer" and "Secondary Manufacturer" and remove the reference to "Primary Manufacturer" from the counteroffer form. The ICR form as currently constructed indicates that a counteroffer must be submitted by a "Primary Manufacturer" of a selected drug. As noted in our comments on CMS' initial Guidance on the Medicare Drug Price Negotiation Program and Information Collection Request for Negotiation Data Elements, Novo Nordisk urges CMS to reconsider this concept considering the significant practical and legal problems that will follow from requiring Primary Manufacturers to collect and report information from Secondary Manufacturers, and to collectively select and submit a counteroffer price. The objections to such an arrangement are obvious and substantial.

Manufacturers of negotiation-eligible drugs should be notified in advance of the selected drug publication date and be given the opportunity to verify and dispute the data used to make a selected drug determination. As it currently stands, CMS will publish the list of ten Part D selected drugs for initial price applicability year (IPAY) 2026 on September 1, 2023. By October 1, 2023, manufacturers of selected drugs must sign an agreement with the Secretary to conduct negotiations, and by October 2, 2023, must submit required data elements for CMS consideration. Given the extremely limited time window in which selected drug manufacturers must compile, prepare, and submit this extensive data set, Novo Nordisk requests that CMS privately notify manufacturers of products that appear on the negotiation-eligible drug list that they could be selected for negotiation at least 30 days prior to the publication of the selected drug list. Manufacturers of negotiation-eligible drugs should be provided a reasonable window of time (e.g., 30 days) to dispute their inclusion on this list (*dispute process discussed further below*). A lack of notice prior to the publication of the selected drug list deprives manufacturers of any reasonable ability to verify or dispute the accuracy of the data CMS used to develop the list in the first place.

CMS should be fully transparent with selected drug manufacturers about the decision-making process behind its initial offer – including the inputs, outputs, considerations, and calculations – to equip manufacturers with enough information to propose a reasonable counteroffer (if desired) and evaluate a rejection of a counteroffer, should that occur. Under the draft guidance, manufacturers have virtually no insight into CMS's methodology behind the development of the initial offer. Novo Nordisk urges CMS to provide manufacturers with the following critical information to evaluate its initial offer, at minimum:

- The selected drug's therapeutic alternative(s) for each indication, data sources used, and the clinical justification for these, ideally before but no later than the selected drug publication date;

- The selected drug's ceiling price and a step-by-step explanation of its calculation, including price points used and assumptions made (if necessary), no later than the provision of the initial offer;
- The CMS-determined "starting point," including how the starting point was calculated (step-by-step), relevant price points and data sources used, no later than the provision of the initial offer;
- A detailed explanation of how CMS analyzed the clinical benefit of the selected drug and arrived at the "preliminary price," including data sources used, outcomes evaluated per indication, and any assumptions made or modeling/calculations that aided the analysis, no later than the provision of the initial offer;
- An account of how information about the patient experience and testimony from patients, providers, caregivers, and other interested stakeholders was evaluated and factored into the decision-making process, no later than the provision of the initial offer;
- A thorough description of how CMS used data submitted by manufacturers on the factors outlined in section 1194(e)(1) to adjust the preliminary price upwards or downwards to form the initial offer, no later than the provision of the initial offer; and
- A mechanism to enable manufacturers to understand and replicate CMS' calculation of the "30-day equivalent supply" of the maximum fair price (MFP) at the National Drug Code level, no later than the provision of the initial offer.

Sharing the above information at this level of detail will be especially important since, as currently proposed, negotiation procedures do not allow for any meetings between manufacturers and CMS until after the counteroffer form is submitted and the counteroffer rejected, and manufacturers have a short window of time to respond to the initial offer. Similarly, when responding to a manufacturer's counteroffer, the Agency should provide a clear and specific explanation of why it does not agree with the proposed counteroffer to enable the manufacturer to effectively prepare a response.

The counteroffer information collection process should allow for consideration of a wide breadth of information, unconstrained by artificial parameters that could inhibit review of the totality of the evidence. In line with CMS' intended use of a "qualitative approach to preserve flexibility in negotiation,"[2] the Agency should eliminate the word limit on the manufacturer counteroffer justification (as well as all free response fields related to manufacturer-specific data) and allow manufacturers the option to upload supplemental documentation in support of their counteroffer. There is no valid reason CMS should prevent manufacturers from providing information relevant to the decision-making process and restricting manufacturers' ability to provide information is contrary to basic principles of reasoned decision-making. Editing the counteroffer justification to meet the proposed 1500-word limit will likely require

[2] https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf

the omission of critical information and detail. Conversely, allowing the submission of supplemental documentation will provide important context that would improve efficiency in the process for both manufacturers and the Agency.

CMS should permit manufacturers of selected drugs for which an MFP is established the opportunity to review CMS' "concise justification" language before it is made public. Advance notice to manufacturers of the justification behind the MFP aligns with CMS' stated goal of transparency in the negotiation program and would enable manufacturers to correct potential errors or flag proprietary information disclosure concerns in advance of publication. Novo Nordisk recommends that a draft of the justification language be shared with selected drug manufacturers as soon as the MFP is published (for IPAY 2026, on September 1, 2024).

Where possible, CMS should reconsider its compressed timeframes throughout the negotiation process. The timeline that is currently proposed for manufacturers to collect and organize such substantial data and evidence requirements into an offer is unrealistically narrow for such a consequential transaction. As noted in our comment letter on the Negotiation Data Elements ICR, Novo Nordisk believes that CMS has flexibility to implement certain timelines, for example, 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 that providing the whole compilation of data requested will be a novel challenge for manufacturers within CMS's extremely limited 30-day timeframe.

Manufacturers should be granted access to a formal dispute resolution process at certain points during negotiation to uphold program integrity and ensure the accuracy of information used throughout CMS' decision-making. The Agency's proposed framework for negotiation leaves manufacturers with inadequate opportunities to respond to and contest CMS' decision-making. Novo Nordisk recommends that CMS allow manufacturers to file disputes during the following time windows during the negotiation process for IPAY 2026:

- Prior to publication of the selected drug list (which would require advanced notification of potential selection – *see above*) – *August 1 – August 30, 2023*
- After the initial offer is made by the Secretary until negotiation meetings end – *February 2, 2024 – June 30, 2024*
- Prior to the publication of the concise justification for the MFP (which would require CMS share a draft of the justification – *see above*) – *September 1, 2024 – September 30, 2024*

CMS should designate a dispute resolution team to review, respond, and adjudicate the dispute in a timely manner (e.g., within 30 days). As a matter of transparency, at the conclusion of each negotiation cycle CMS should issue a public report with aggregated statistics on the

dispute process – for example, the number of disputes, number of favorable and unfavorable determinations, or other metrics – related to disputes at all the time points mentioned above.

Novo Nordisk appreciates the opportunity to comment on CMS's *IRA Drug Price Negotiation Process* for IPAY 2026. Given the unprecedented change brought about by these policies, we urge the Agency's consideration of these 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.

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June 20, 2023

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: Information Collection Request (ICR) Form for Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10849, OMB 0938-NEW) ("Counteroffer form")

Dear Mr. Parham:

On April 18, 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 draft guidance published by CMS on March 15, 2023 in which it describes the negotiation process for selected drugs, among other topics ("the draft guidance").[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.[4] 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. Our comments below address both fields of the draft data collection form.

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[1] 88 Fed. Reg. 23860, April 18, 2023.
[2] CMS. "Drug Price Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (IRA)." Available at https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10849.
[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)
[4] SSA 1194(c) defines the price floor and price ceiling as the lower of average enrollment weighted net price of the selected drug, and a time-based calculation based upon its non-Federal Average Manufacturer Price (non-FAMP).

Pharmaceutical Care Management Association
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1. **CMS Should Expect and Entertain Vociferous Primary Manufacturer Responses to Its Initial Offers**

Per the guidance, CMS will allow manufacturers of selected drugs to submit a written counteroffer within 30 days of receipt of CMS's initial offer. CMS would receive written counteroffers from Primary Manufacturers through the Health Plan Management System. The counteroffer must provide a price per 30-day equivalent for the drug and respond to CMS's written justification for its initial offer. This response is limited to 1,500 characters (approximately 300 words). It must also be signed by the Primary Manufacturer's CEO or other specifically designated official for entering into the agreement with CMS. Following submission of the written counteroffer, CMS and manufacturers will exchange further offers and counteroffers until one party agrees to the other's written document.

According to the draft guidance and other published timelines, CMS will form its initial offer based on information submitted by primary manufacturers and the interested public between October 2, 2023 and January 31, 2024. CMS is not limited to information submitted to it, however, and can base its initial offer on any number of other enumerated variables in the statute. Final maximum fair prices (MFP) will be published on September 1, 2024 for the initial price applicability year (2026). The period following the announcement of the list of selected drugs will see an explosion of commentary in the public domain, both peer-reviewed and otherwise, that may argue in favor of or against CMS's eventual initial offer on any given selected drug.

While any research available prior to September 1, 2023 will likely to have been submitted during the initial offer construction period (from October 2, 2023 through January 31, 2024), CMS should allow primary manufacturers to highlight specific peer-reviewed studies including those that were not yet published by the time of this initial data submission, as a part of its written counteroffer. CMS should grant the public – through primary manufacturers – a grace period of sorts to submit additional information. CMS can also rely on additional published sources, in response to counteroffers. There is plenty of time for CMS to entertain the justifications provided by manufacturers between the close of the counteroffer period (ending March 1, 2024) and the publication date for the final MFPs (September 1, 2024). Cutting off public feedback at 300 words is not providing sufficient space for the public to engage with CMS on its proposed pricing. **Therefore, we strongly encourage that CMS expand the free text field to respond to CMS's initial offer to more than 1,500 characters, and to allow for the submission of attachments, as well.**

2. **Manufacturers May Not Have Enough Information to Respond with a Counteroffer for a 30-Day Equivalent**

As described in CMS's initial negotiation program guidance,[5] qualified single source drugs include all dosage forms and strengths of the underlying active moiety. For its initial offer, CMS will provide a single price for a 30-day equivalent supply of the "selected drug." We find this approach confusing because it tries to tie pricing to a product's ultimate use, rather than the contents of the package. Without pegging the initial offer to a specified dosage form or strength, but instead to a perceived length of therapy, manufacturers may be unwilling or unable to

[5] See footnote 3.

calculate the appropriate pricing. Many dosage, form, strength, and quantity packages (e.g., NDC-11 configurations) could be used for any number of days supplied, either depending on the patient's size, indicated use, or other lab or clinical values (e.g., using a lower dose to manage side effects). **We recommend that CMS's initial offer to manufacturers be accompanied by a price sheet for all, or at least the highest volume, NDC-11s for the selected product. This counteroffer form (the subject of this letter) should then be accompanied by a similar response sheet from the manufacturer.** They would be required to fill in the expected pricing for each package, so there is no miscommunication about 30-day equivalents. This will allay any concerns that the manufacturer is offering a price that doesn't match the actual products it offers in the marketplace.

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. We hope our suggestions help CMS finalize data elements to be collected from manufacturers. CMS's goals should include making sure the public feels fully engaged, and that the data received by CMS is subject to the least amount of interpretation as possible. 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.

* * * *

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
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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-----
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June 20, 2023

VIA ELECTRONIC FILING - REGULATIONS.GOV

Meena Seshamani, M.D., Ph.D.
CMS Deputy Administrator and Director of the Center for Medicare
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Re: Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849, OMB, 0938-NEW)

Dear Deputy Administrator Seshamani:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit comments in response to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act* (ICR or the ICR), including the Federal Register Notice, Supporting Statement – Part A, and the ICR Form (Counteroffer Form) (CMS-10849, 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.

Under the "Medicare Drug Price Negotiation Program" (the Program) established in Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (P.L. 117-169), codified in Sections 1191 through 1198 of the Social Security Act (SSA or the Act), a manufacturer of a selected drug may opt to submit a written counteroffer within 30 days of receipt of a written initial offer from CMS as part of the process the agency employs to set a "lowest maximum fair price" as required under the Act. The ICR and Counteroffer Form set forth the process and format CMS intends to follow for operationalizing the counteroffer process. Below we discuss several substantive and procedural concerns with the ICR and Counteroffer Form and recommend revisions to address them, including:

(1) Eliminating the primary/secondary manufacturer construct proposed by CMS;

(2) Developing a process for earlier, more effective communication between the manufacturer and CMS by providing for meetings earlier in the process;

[1] 88 Fed. Reg. 23,680 (Apr. 18, 2023); Centers for Medicare and Medicaid Services (CMS), Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act (CMS-10849, OMB, 0938-NEW), Supporting Statement – Part A (Apr. 18, 2023), https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10849; CMS, Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act, ICR Form (Apr. 18, 2023), https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10849.

(3) Creating a tool to provide information on the "30-day equivalent supply" so manufacturers can assess potential maximum fair prices (MFPs) at the level of specific National Drug Codes (NDC);

(4) Developing a template for the "concise justification" CMS will provide as part of its initial offer, so the manufacturer can understand how evidence and factors informed the offer;

(5) Eliminating the word limit on the manufacturer counteroffer justification;

(6) Modifying the certification requirement so it is not unduly burdensome;

(7) Recalculating the reporting burden estimate; and

(8) Ensuring that any proprietary information is protected in accordance with statutory requirements.

Eliminate the Primary/Secondary Manufacturer Construct

Consistent with our April 14th comments (attached with this submission as Appendix A) on CMS' initial Guidance[2] (Guidance, or the Guidance) on the Medicare Drug Price Negotiation Program and May 22nd comments (attached with this submission as Appendix B) on CMS' draft Information Collection Request for Negotiation Data Elements[3] (Negotiation Data Elements ICR), PhRMA strongly recommends that CMS eliminate the "Primary/Secondary" manufacturer construct in its entirety from the Program, including in the counteroffer process. The ICR Form indicates that a counteroffer must be submitted by a "Primary Manufacturer" of a selected drug. To the extent that more than one entity satisfies the IRA's definition of "manufacturer" for a selected drug, CMS plans to designate the entity that holds the New Drug Application(s) (NDA(s))/Biologics License Application(s) (BLA(s)) for the drug to be the "Primary Manufacturer."

"Primary Manufacturers" legally do not have access to "Secondary Manufacturer" information and, thus, the proposed Primary/Secondary Manufacturer policy contemplated in the Guidance should be eliminated. As Primary Manufacturers will not be able to procure and certify to information from Secondary Manufacturers, CMS is proposing an unrealistic standard that will often be impossible for manufacturers to meet. CMS should instead enter into separate agreements with each entity that satisfies the definition of manufacturer to obtain any essential information throughout the MFP setting process, including as it pertains to the counteroffer process.

Develop Process for Earlier, More Meaningful Manufacturer Engagement, Including Meetings Prior to the Counteroffer

In the Guidance and ICR, CMS proposes to allow up to three potential in-person or virtual meetings between a manufacturer and CMS as part of the MFP decision-making process, but only at the end of the process in instances where a manufacturer's written counteroffer is not accepted by CMS. Meetings at this stage, while useful, come far too late in the process to enable communication between the manufacturer and CMS that will be essential at earlier stages of the process. As recommended in prior comments, PhRMA urges CMS to revise its process to allow earlier, more meaningful manufacturer engagement to include meetings *before* the counteroffer stage of the process. Earlier meetings will be particularly important given the broad range and disparate types of data from manufacturers and public stakeholders that will factor into MFP decision-making, as well as the difficulty CMS will face in

[2] *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*

[3] 88 Fed. Reg. 16,983 (Mar. 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 (Mar. 21, 2023), https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847; CMS, Information Collection Request for Negotiation Data Elements under Section 11001 and 11002 of the Inflation Reduction Act, ICR Form (Mar. 21, 2023), https://www.cms.gov/regulations-and-guidance/legislation/paperworkreductionactof1995/pra-listing/cms-10847..

evaluating submitted data and conveying it to the manufacturer in a timely way. Given the broad range of data required throughout this price setting process, we also would encourage CMS to consider notifying manufacturers that their drugs are being considered for selection prior to the formal public announcement and initiation of the information collection request. As discussed in Section III.h. of our Guidance comments, PhRMA recommends that CMS offer manufacturers the opportunity to meet a minimum of three times *prior to* a counteroffer, including after drug selection but prior to initiation of the price setting process; prior to presentation of an initial offer; and, after presentation of the initial offer. PhRMA requests that CMS consider the concerns we raised in our comments on the Guidance, including, but not limited to, the insufficient number of meetings in the price setting process.

Create a Tool or Spreadsheet for Manufacturers to Evaluate How a Proposed MFP for a Selected Drug's "30-Day Equivalent Supply" Breaks Down by National Drug Code (NDC)

The Counteroffer Form requires manufacturers to submit a price for a selected drug in the form of a "single price per 30-day equivalent supply." The Form indicates that this format should be used "rather than unit – such as tablet, capsule, injection – or per volume or weight metric" and should be weighted across dosage forms and strength, as applicable. PhRMA reiterates the request from Section III.m. of our comments on the Guidance for CMS to provide better clarity as to how CMS plans to compute 30-day equivalent supplies to aid manufacturers in understanding the Agency's application of a single Maximum Fair Price (MFP) across dosage forms and strengths. We urge CMS to provide manufacturers with CMS' calculated 30-day equivalent supply for each NDC-9; the total number of units dispensed for each NDC-9 in the 2022 Part D Prescription Drug Event (PDE) data; and an electronic tool or Excel spreadsheet with CMS' 10-step calculation approach for applying the MFP across different dosage forms and strengths. Given the novelty of the program, the complexity of CMS' calculation, and the need to verify data inputs, it is imperative that manufacturers be able to review both the data and calculation methodology used by CMS.

Include in the ICR a Template that Describes How Submitted Data and MFP Factors Influenced CMS' Initial Offer

CMS notes in the proposed Counteroffer Form that it will provide a manufacturer with a "concise justification" for its initial offer based on factors described in Section 1194(e), as required by the SSA. This justification will play an important role in a manufacturers' consideration and development of a counteroffer, but the agency provides no detail on what it will or will not include in its concise justification. CMS should revise the ICR to include a template that will be used by the agency to provide the "concise justification" for its initial offer at a level that enables manufacturers to understand how data and MFP factors influenced the agency offer. Because these evaluations will need to occur on an indication-specific level (as reflected in CMS' Guidance), the template should convey summary information on data and factors on an indication-by-indication basis. As discussed in Section III.j. of our comments on the Guidance, PhRMA recommends that the template include information similar to the final published explanation, and that such justifications identify key pieces of information, including:

- Therapeutic alternative(s) for a selected drug (for each indication) and the rationale for selecting each therapeutic alternative;
- How CMS calculated the ceiling price;
- CMS's starting point and how it established this starting point;
- How each of the factors listed in section 1194(e) were weighed relative to one another in CMS' decision-making and details on how the starting point was adjusted upwards or downwards based on these factors;

- Data and analysis CMS developed and considered supporting each factor, including evidence provided by third parties CMS engaged formally or informally;
- If any data or evidence considered by CMS was generated from a study that referenced or relied on the Quality-Adjusted Life-Year (QALY) or other potentially discriminatory metrics;
- Benefits and impacts of a selected drug CMS considered; and
- Stakeholders (e.g., patients, caregivers, clinicians, and manufacturers), and other government agencies and organizations CMS engaged, formally or informally, including how stakeholder input explicitly informed CMS' determination of the MFP and selection of each therapeutic alternative.

We also believe that CMS should release information on the data and analysis that CMS received formally and informally (e.g., non-proprietary information on comparative effectiveness of treatments received through the Data Elements ICR process) but chose to not include in its determination of MFP as part of the initial justification. CMS should also outline any remaining questions or uncertainties that arose while formulating the initial offer. This information will allow manufacturers to be more responsive to CMS and tailor their counteroffer response to the information CMS deems most relevant and/or make the case for why CMS should reconsider information that may be particularly important to key stakeholders including patients and caregivers.

This detail and template are essential since the manufacturer must provide a justification in its counteroffer through a "Free Response" box that comprehensively responds to CMS' reasoning in the Agency's initial offer. As with the manufacturer justification of its counteroffer (addressed below), it is important for CMS to provide adequate detail in its concise justification of the initial offer. The statutory requirement to provide a "concise" justification simply means that the Agency should not include extraneous, unnecessary detail, but it does not permit an incomplete justification, and it does not relieve the Agency of the responsibility to explain how it considered, evaluated, and weighted each factor in deciding on an initial offer. CMS should provide more information on the substance of the template it will use for providing the initial justification and ensure it allows manufacturers to understand how various factors influenced the initial offer for different indications. CMS should also allow manufacturers the ability and sufficient time to review and refute the contents of CMS' justification before it is made public.

Eliminate Word Limit on Manufacturer Counteroffer Response

PhRMA urges CMS to eliminate all word limits across the data submission process including the 1,500-word limit on a manufacturer's justification of its counteroffer in the "Free Response" portion of the Counteroffer Form. A 1,500-word limit equals only about 2.5 pages. Based on the breadth of data CMS seeks for manufacturers to submit and the requirement for manufacturers to provide a justification for a counteroffer based on these factors, a response limited to 1,500 words will not allow for a meaningful response that covers the essential elements that are to be considered in the process. Manufacturers will inevitably be required to eliminate key details to meet the word limit requirement. Given the potential widespread impacts on patients and innovation from the MFP process, CMS would benefit from being able to evaluate the full scope of data on each selected product and therapeutic alternatives. Thus, CMS should remove any limitations on the breadth and type of data submitted by manufacturers when data is both initially shared with CMS and as part of this counteroffer process. Additionally, similarly to Negotiation Data Elements ICR, CMS should provide space for manufacturers to attach studies or other key pieces of information that support the manufacturer's counteroffer response.

Modify the Certification Requirement

The Certification statement of the Counteroffer Form requires manufacturers to certify that the submission is "complete and accurate" and requires manufacturers to "timely notify CMS" if information submitted has changed. In addition, it requires signing a statement regarding liability under the False Claims Act. In alignment with our comments on the Negotiation Data Elements ICR, CMS should modify the terms of the certification to require all submitters to agree that information is accurate and prepared *in good faith and after reasonable efforts*, with no requirement for completeness. If CMS retains the requirement for completeness, at a minimum "complete" should be defined to mean all sections of the form have been filled out. It is simply not rational to require a certification to completeness and accuracy when CMS bases the counteroffer process on negotiation factors for which the Agency seeks an extensive set of data while simultaneously limiting the number of words in the "Free Response." Furthermore, as noted above and in previous comments to CMS, in some cases "Primary Manufacturers" legally do not have access to "Secondary Manufacturer" information which makes it impossible for "Primary Manufacturers" to certify the accuracy and completeness of this data.

CMS also should remove the requirement of timely notification of changed information to avoid unintended noncompliance of the certification and unnecessary burden. This term of the certification, with no specification of the applicability of a time limit, adds an ongoing burden for submitters. Given the ongoing nature of scientific discovery and clinical research, data on cost and evidence on the uses of medicines (both for a selected drug and treatment alternatives) will continue to evolve over time and that new data will continually become available. Taken literally, CMS' requirement would mean that respondents would have an ongoing obligation to regularly update the counter-offer explanation to represent the most current scientific discoveries and evidence. We do not believe CMS intends such a burdensome obligation; nor that CMS is authorized to threaten penalties for failure to engage in these ongoing updates. We urge CMS to excise the "changed information" requirement from its collection.

Recalculate Reporting Burden Estimate, Which Likely is a Significant Underestimate

CMS estimates a total burden of 792.5 hours (79.25 hours * 10 respondents) and a total cost of $99,870.10 ($9,987.01 per respondent * 10 respondents) for manufacturer completion and submission of information in the Counteroffer Form. CMS explains it expects each manufacturer respondent will use a team of lawyers, health care professionals, economists, and business operation specialists to complete the form. PhRMA requests that CMS recalculate this reporting burden estimate, which we view as significantly underestimating the total actual burden and cost of responding based on the breadth of data to be considered as a result of this ICR and business operations required to evaluate counteroffer options. The estimated burden and cost also raise questions about the substantive nature of the "concise justification" CMS intends to provide to manufacturers as part of the price setting process, as well as concerns about the comprehensiveness of such justification, if each manufacturer respondent's response is anticipated to require only 79.25 hours to complete. Notably, CMS' estimate of its own costs and hours (in Table 2 of the Supporting Statement) appears to assign significantly more time to the Agency than to the manufacturers who will be gathering, presenting, and distilling counter-offer information.

Ensuring That Any Proprietary Information is Protected in Accordance with Statutory Requirements

As discussed in our previous comments on the Guidance and the Negotiation Data Elements ICR, protection of manufacturer confidential data is critically important. We note that it is likely that manufacturers may submit proprietary data to CMS to help justify the submitted counteroffer. As such, 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. Please see Section I.d. of our Guidance comments for additional recommendations and feedback on the need for CMS to protect proprietary information.

Conclusion

PhRMA appreciates the opportunity to submit comments in response to the *Information Collection Request for Drug Negotiation Process under Sections 11001 and 11002 of the Inflation Reduction Act*, including the Federal Register Notice, Supporting Statement – Part A, and the ICR Form. PhRMA urges CMS to carefully consider our recommendations for revising the Counteroffer Form and related process.

Please feel free to 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.

Sincerely,

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