

APPENDIX A.

April 14, 2023

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Centers for Medicare & Medicaid Services
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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 insert]. 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

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

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/pralisting/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,

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 not 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 data³⁷, 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/practicing/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

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 Act⁵⁹ 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.

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 individuals⁶¹ “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 the SSA.⁸⁸ This prohibition would prevent CMS from using QALYs as part of its determination of MFPs, including 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

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 population⁹⁶ 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-occlusive 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

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/encr.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 domains¹⁰⁸ 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 principles¹¹⁰ 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*

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 concerns¹¹⁵), 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/doi/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 subgroup¹²¹ – defined by PD-L1 expression – because overall survival can increase by as much as 164 percent¹²² 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

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, Jyda 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](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

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. Available 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.

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 time¹⁴⁵), 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 2020¹⁵⁰ 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 price¹⁵² 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.

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 meet¹⁶⁰ 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. Patients¹⁶¹ 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

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/doi/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.

I. 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.

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 (c)(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 <u>December 31, 2025</u> (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 <u>January 1, 2026</u> 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 Plan¹⁹⁵ 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.

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 302.5 (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 MFP¹⁹⁸ – 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

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%942013%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.

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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)