April 14, 2023

VIA ELECTRONIC DELIVERY

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

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

The Council of State Bioscience Associations (CSBA) is a coalition of independent state and territory based non-profit trade associations, each of which advocates for public policies that support responsible development and delivery of innovative life-sustaining and life-saving biotechnology solutions. Convened by the Biotechnology Innovation Organization (BIO), CSBA's collective voice represents the true grassroots network of innovators, researchers, manufacturers and accelerators across the country. According to a recent industry report, U.S. bioscience industry employment in 2021 reached 2.1 million jobs in more than 127,000 businesses across every state in the U.S. and Puerto Rico. The total economic impact of the bioscience industry on the U.S. economy, as measured by overall output, totaled $2.9 trillion dollars in 2021.[1] (TEConomy/BIO, 2022)

The majority of CSBA's member companies are research-intensive small and large biotechnology companies working on cutting-edge innovations. Most of these are pre-revenue human health companies that take enormous risks to develop the next generation of biomedical breakthroughs. Their pipelines have the potential to benefit millions of patients suffering from diseases for which there are no cures or treatments.

We are gravely concerned about the impacts the IRA will have on companies' investments in research and development, as well as the downstream impact on beneficiary access to future treatments and cures. We are especially concerned that treatments for rare diseases, complex medical conditions and those areas with high unmet need will be shelved in favor of treatments that are less likely to be subjected to negotiation.

As such, the CSBA Board of Directors writes today to endorse BIO's formal comments on the Medicare Drug Price Negotiation Program, which are appended to this letter.

[1] TEConomy/Biotechnology Innovation Organization. (2022). *The U.S. Bioscience Industry: Fostering Innovation and Driving America's Economy Forward.* https://www.bio.org/csba-resources-and-reports

We look forward to continuing to work with the Agency on these important issues. Should you have any questions, please do not hesitate to contact Michele Oshman, Executive Director for CSBA and Vice President of External Affairs at BIO, at 202-215-8140 or moshman@bio.org.

Sincerely,

Michele Oshman (Apr 14, 2023 10:54 EDT)

Michele M. Oshman
Executive Director, Council of State Bioscience Associations
Vice President, External Affairs
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Maria Thacker Goethe
Maria Thacker Goethe (Apr 14, 2023 10:57 EDT)

Maria Thacker
Chair, Council of State Bioscience Associations
CEO, Center for Global Health Initiatives and Georgia Bio

John Conrad
Vice Chair, Council of State Bioscience Associations
Illinois Biotechnology Innovation Organization

Attachment:
BIO Comments: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments

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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

The Biotechnology Innovation Organization (BIO) appreciates this opportunity to comment on the initial guidance regarding the Drug Price Negotiation Program (Negotiation Program) under the Inflation Reduction Act of 2022 (IRA) issued by the Centers for Medicare & Medicaid Services (CMS or Agency) on March 15, 2023 (Initial Guidance).[1]

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, delay the onset of such diseases, or prevent them in the first place. As a result, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes but also have reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO's members include biologic and vaccine manufacturers, which have worked closely with stakeholders across the spectrum, including the public health and patient advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

BIO appreciates the steps the agency has taken to establish a dialogue with key stakeholders about the Negotiation Program and other elements of the IRA, but we have significant concerns about the Initial Guidance and the limitations on comments CMS has imposed.

We also believe it's imperative to underscore our views on the IRA. We have long supported a Medicare Part D out-of-pocket cap and the ability for patients to spread these costs throughout the year. These

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

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are essential patient protections. At the same time, we believe that patient out-of-pocket costs will never be truly addressed unless the broken rebate system – which benefits pharmacy benefit managers (PBMs) over patients – is addressed. PBMs continue to leverage their size and market influence to ensure they can rake in enormous profits, and they do so at the expense of vulnerable patients.

In addition, we are very concerned about the significant and negative impacts the IRA will have on companies' investments in research and development, which in turn will harm beneficiary access to future treatments and cures, particularly for rare, hard-to-treat diseases and those areas with high unmet need. We continue to urge CMS to consider these impacts as the agency works to update this proposed guidance based on stakeholder feedback.

We also note our strong disappointment that key aspects of this guidance have been issued as final without soliciting comment, which is a concerning step backward from CMS's stated commitment to transparency. BIO strongly urges the Agency to consider stakeholder comments on all aspects of the Initial Guidance. Notably, despite previously committing to "prioritiz[ing] transparency and robust engagement" in its implementation of the Negotiation Program,[2] the Agency solicits comment on only certain policies, and finalizes other policies with no opportunity for comment—specifically, the foundational policies set forth in Section 30 of the Initial Guidance.[3] The Agency's own stated goals of transparency and engagement require immediate reconsideration of this ill-advised start to the Agency's stewardship of the Negotiation Program.

BIO and our members have long argued that the underlying structure of the negotiation program, as set forth by the statute and implemented here by CMS, is legally flawed. In review of the punishing penalties for non-compliance, and the general inflexibility of the process for product selection and maximum fair price (MFP) implementation, these legal flaws cannot be overcome through general guidance clarity at this stage. Nevertheless, we provide herein several suggestions for CMS to consider that might be helpful in the transparency objective of the Agency as it implements this program. None of these resolve the more fundamental legal infirmities of the overall program, nor could they.

We outline below how the implementation of the Negotiation Program would materially benefit from two-sided engagement on all topics, including both a full opportunity for stakeholders to submit comments on proposed policies and meaningful responses to such comments that demonstrate the Agency's consideration of the points made and reveal the reasoning underlying the Agency's final

[2] CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 (Jan. 11, 2023), *available at* https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf.

[3] While BIO understands that the policies set forth in Section 30 of the Initial Guidance are final and that CMS is not soliciting comment on such policies, BIO sets forth herein for the record the comments that it would have made had CMS solicited comment.

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decision-making. Such an approach would fulfill the purpose of a comment period: to enable "[t]he interchange of ideas between the government and its citizenry[, which] provides a broader base for intelligent decision-making and promotes greater responsiveness to the needs of the people."[4] The need for such a fulsome process is especially acute here, given the novelty and complexity of the Negotiation Program; the vast ramifications that the program will have for patients, providers, pharmacies, manufacturers, and countless other stakeholders; and the potentially profound negative repercussions for patient access to needed therapies that could follow from errors, misunderstandings, or gaps in understanding. In these circumstances, the Agency should maximize transparency and engagement in its decision-making process, including by both affording a full opportunity for comment and meaningfully responding to stakeholder feedback.

This includes ensuring the negotiation process is transparent, predictable, and fair, with CMS providing necessary accountability to stakeholders and clarifying how it will consider and utilize the broad set of information it will collect and review related to the negotiation factors. Further, we continue to urge CMS to emphasize factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

We also urge CMS to eliminate its proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings Moreover, BIO opposes the blanket prohibition on manufacturers from disclosing or otherwise publicizing information "in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers…". This one-sided information control heightens the ultimate public complaint that the entirety of the "negotiation" process is anything but actual "negotiation." BIO disagrees with this approach and recommends CMS abandon it.

We also recommend that CMS finalize the Initial Guidance well in advance of the selected drug publication date for initial price applicability year (IPAY) 2026 to ensure that all stakeholders have ample time before such date to fully digest the contents of the finalized guidance and conform their actions accordingly. Similarly, CMS should solicit comment on proposed guidance applicable to IPAY 2027 and IPAY 2028 (the first IPAY applicable to Medicare Part B drugs) as soon as reasonably possible and well in advance of the selected drug publication dates for such IPAYs.

[4] *Buschmann v. Schweiker*, 676 F.2d 352, 357 (9th Cir. 1982) (internal quotation marks and citations omitted).

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Below please find an overview of our recommendations; our more detailed comments follow.

Regarding the definitions of qualifying single source drugs and negotiation eligible drugs:

- BIO strenuously disagrees with CMS's approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.
- CMS should clarify the scope of the orphan drug exclusion in a manner that maximizes protections for orphan drugs.
- CMS should take steps to make the process to qualify for the small biotech exception more transparent and predictable.

Regarding the selection, and delayed selection, for negotiation, CMS should:

- Provide for a pre-selection process where, well in advance of the selected drug publication date, CMS would notify each manufacturer of each drug that it intends to select for negotiation and afford each manufacturer a dispute process.
- Improve the process by which a biosimilar manufacturer may request a delay in the selection of a reference product for negotiation due to anticipated biosimilar market entry. This includes providing a meaningful opportunity to request a delay, allowing for a dispute resolution process, and considering all information submitted by a biosimilar manufacturer.

In implementing the negotiation process, CMS should:

- Provide for robust and meaningful engagement and dialogue between the Agency and the manufacturer throughout the negotiation process.
- Allow manufacturers to supplement timely submissions where a post-submission development arises or there otherwise is good cause.
- Provide a meaningful justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.
- Provide more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process.
- Withdraw its overly broad confidentiality obligations imposed on manufacturers.

In setting the MFP, CMS should:

- Impose on itself bright-line limitations that mitigate the negative effect of the MFP on patient access and on therapeutic innovation.
- Commit to setting the MFP at a price that will not imperil patient access.

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- Ensure that the MFP is not set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.
- Ensure that the MFP is not set below the MFP ceiling during any year of the price applicability period into which patent protection extends.
- Ensure that the MFP is set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.
- Ensure the MFP is not set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC).
- Ensure predictable, transparent engagement with manufacturers regarding how the MFP was set.

In utilizing the negotiation factors, CMS should:

- Ensure a transparent, fair, and predictable process.
- Emphasize factors related to clinical benefit and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.
- Utilize a more robust definition of unmet medical need.
- Clarify how it will evaluate the evidence about alternative treatments by different stakeholders and how different evidence will be considered in setting the MFP.
- Ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.
- Allow manufacturers to use reasonable assumptions regarding the information they submit on the manufacturer-specific data.
- Reject approaches that would reduce the preliminary price when a drug has available patents and exclusivities.
- Eliminate reporting and other requirements under the Primary Manufacturer/Secondary Manufacturer Construct.

In establishing the MFP Ceiling, CMS should:

- Abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP.
- Establish an exceptions process to account for restatements and anomalies.
- Confirm if the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY or the selected drug publication date.
- Calculate the MFP ceiling for Part D drugs exclusive of manufacturer price concessions unless they are passed through at the point of sale.

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Regarding the requirement that manufacturers provide access to the MFP, CMS should:

- Finalize its proposal that access to the MFP may be provided through an MFP rebate model.
- Utilize a CMS-established third-party administrator (TPA) or clearinghouse.
- Clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.
- Condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use claims modifiers.
- Finalize its proposals that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.
- Define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).
- Simplify its approach for applying the MFP across dosage forms and strengths and address concerns with its proposed methodology.
- Abandon its bona fide marketing standard and instead adopt a standard that consistently designates the MDRP "market date" as both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

In addition, we recommend that CMS:

- Clarify that selected drugs are not subject to an inflation rebate.
- Amend its regulatory definition of "unit" to exclude MFP units from the ASP calculation.
- Proceed with caution on the implementation of CMPs and allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed.
- Ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date.
- Abandon its "Primary Manufacturer" and "Secondary Manufacturer" construct as part of the Agreement as it is impracticable and has no legal basis.
- Protect beneficiary access to needed therapies, including selected drugs, and implement safeguards to ensure such access.

I. Qualifying Single Source Drugs and Negotiation-Eligible Drugs

A. Background

Section 1192(e) of the Social Security Act (SSA) generally defines "qualifying single source drug" to mean:

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- A drug product approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and marketed pursuant to such approval where at least seven years have elapsed since the date of such approval and there is no approved and marketed generic for such product;[5] and
- A biological product approved under section 351(a) of the Public Health Services Act (PHSA) and marketed pursuant to such licensure where at least eleven years has elapsed since the date of such licensure and there is no licensed and marketed biosimilar for such product.[6]

The statute provides for certain exclusions from the definition of "qualifying single source drug"—certain orphan drugs,[7] plasma-derived products,[8] and certain low Medicare spend drugs.[9]

Section 1192(d) generally defines "negotiation-eligible drug" to mean, with respect to an IPAY:

- Each of the top fifty qualifying single source drugs by Medicare Part D expenditures over a specified twelve-month period; and
- Starting with IPAY 2028, each of the top fifty qualifying single source drugs by Medicare Part B expenditures over a specified twelve-month period.[10]

The statute provides for the exclusion of a "small biotech drug" from the definition of "negotiation-eligible drug" for IPAYs 2026, 2027, and 2028.[11] Section 1192(d)(2) generally defines "small biotech drug" to mean a qualifying single source drug for which:

- The drug's 2021 Part B or D expenditures are equal to or less than one percent of all drugs' 2021 Part B or D expenditures; and
- The drug's 2021 Part B or D expenditures are equal to or more than eighty percent of its manufacturer's drugs' 2021 Part B or D expenditures.[12]

The statute provides for the exclusion of "[a] new formulation, such an extended release formulation" from the definition of "small biotech drug."[13]

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[5] SSA § 1192(e)(1)(A) (the seven years are counted to the selected drug publication date with respect to the applicable IPAY).
[6] *Id.* § 1192(e)(1)(B) (the eleven years are counted to the selected drug publication date with respect to the applicable IPAY).
[7] *Id.* § 1192(e)(3)(A).
[8] *Id.* § 1192(e)(3)(C).
[9] *Id.* § 1192(e)(3)(B).
[10] *Id.* § 1192(d)(1).
[11] *Id.* § 1192(d)(2). The statute also provides for a Maximum Fair Price (MFP) floor for a "small biotech drug" for IPAYs 2029 and 2030. *Id.* § 1194(d).
[12] *Id.* § 1192(d)(2)(A).
[13] *Id.* § 1192(d)(C).

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B. Distinguishing among qualifying single source drugs and dosage forms and strengths of such drugs

It is imperative that CMS reconsider its approach to identifying a qualifying single source drug and its dosage forms and strengths by reference to common active moiety (drugs) or common active ingredient (biologics), and instead identify such a drug and its dosage forms and strengths by reference to common New Drug Application (NDA) or Biologics License Application (BLA).[14]

In the Initial Guidance, CMS states that it will treat products as the same qualifying single source drug where, for drug products, they share the same active moiety or, for biological products, they share the same active ingredient, and the same manufacturer holds all applicable NDAs or BLAs.[15] This policy is irreconcilable with the statute.

The statute requires products to be treated as the same qualifying single source drugs only where they share the same NDA or BLA. This necessarily follows from the plain text of section 1192(e)(1). As set forth above, "qualifying single source drug" is defined for products approved under an NDA by reference to whether seven years has elapsed since "such approval;"[16] likewise, the term is defined for products licensed under a BLA by reference to whether eleven years has elapsed since "such licensure."[17]

Congress's use of "such license" and "such approval" in the statute is intentional, unambiguous, and must be given effect. Congress used this language to denote that a qualifying single source drug is distinguished by a distinct approval or licensure—i.e., a distinct NDA or BLA. CMS has no authority to re-write the plain language of the statute by inventing an ultra vires distinction between qualifying single source drugs based on their applications. Where "Congress has been unambiguous, neither the Agency nor [a] court may diverge from that intent."[18]

Although the plain language of the statute is dispositive, BIO notes that other canon of statutory construction confirm Congress's unambiguous intent to distinguish qualifying single source drugs based on distinct NDAs or BLAs and to mandate that drug and biologic products would not be subject to price controls unless a sufficient time has elapsed since "such approval" (7 years) or "such licensure" (11 years).[19] Of particular note, the statute defines "qualifying single source drug" by express reference to

[14] For a discussion of the related and equally critical concern with CMS's "bona fide marketing" standard, please see section VI.F.
[15] Initial Guidance at 8.
[16] SSA § 1192(e)(1)(A).
[17] *Id.* § 1192(e)(1)(B).
[18] *Cabazon Band of Mission Indians v. Nat'l Indian Gaming Comm'n*, 827 F. Supp. 26, 29 (D.D.C. 1993), *aff'd*, 14 F.3d 633 (D.C. Cir. 1994).
[19] *See Chevron v. Nat'l Res. Def. Council*, 467 US 837, 843 n.9 (1984) (in addition to the plain text, the traditional tools of statutory construction are used to ascertain the intent of Congress).

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the FDCA and PHSA. It is well understood that a statute should be interpreted in the manner "most compatible with the surrounding body of law into which the provision must be integrated."[20]

CMS should therefore look to the well-established framework under the FDCA and PHSA for distinguishing among products. Under this framework, drug and biological products generally may be marketed only if approved or licensed by FDA,[21] and manufacturers seeking such approvals or licensures must meet stringent requirements bearing on safety, effectiveness, and other considerations.[22] In implementing this framework, FDA has spoken directly to the circumstances under which a change to an existing product is so significant that it yields a new product warranting a new NDA or BLA is, as well as the circumstances under which a change to an existing product is not.[23] It is manifestly reasonable and appropriate to rely on such FDA standards here, such that a product approved or licensed under a new NDA or BLA is a distinct qualifying single source drug.

There are immeasurable benefits to giving effect to the statute as written and, as Congress intended, adopting FDA's application-based framework for distinguishing products (as opposed to CMS's newly invented, statutorily unmoored scheme for doing so). First, and most critically, doing so would avoid exacerbating the disincentive to develop next-generation therapies inherent in the Negotiation Program to the point of suffocating all such innovation, to the detriment of patients in need. The sheer breadth of CMS's "qualifying single source drug" definition—which amalgamates drug products by common active moiety and biological products by common active ingredient—leaves no incentive for therapeutic advancement and will have significant, negative impacts on innovation for years to come. Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways, and modes of administration to achieve maximum clinical benefit for patients. Researchers cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is harming investments into new therapies, including for orphan and hard to treat diseases. For the sake of pharmaceutical and biotechnology innovation, and patient access to needed therapies, CMS's current framework cannot stand.

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[20] *Green v. Bock Laundry Machine Co.*, 490 U.S. 504, 528 (1989) (Scalia, J., concurring); *cf. Erlenbaugh v. United States*, 409 U.S. 239, 243–44 (1972) (under the rule of *in pari materia*, it is generally "assume[d] that whenever Congress passes a new statute, it acts aware of all previous statutes on the same subject").

[21] 21 U.S.C. § 355(a); 42 U.S.C. § 262(a)(1)(A).

[22] 21 U.S.C. § 355(c), (d); 21 C.F.R. §§ 314.105, 314.125 (NDA requirements); 42 U.S.C. § 262(a)(2)(C); 21 C.F.R. §§ 601.2(a), 601.4(a) (BLA requirements).

[23] FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees (Dec. 2004), *available at* https://www.fda.gov/media/72397/download. For example, a new active ingredient (e.g., a different salt, ester, or complex of an approved moiety) should be approved under a new application. *Id.* at 3. In contrast, a new strength generally should be approved under a supplement. *Id.* at 4. The same is true for a new container size or package type of the same indication and route of administration. *Id.* Certain changes in dosage form and route of administration should be approved under a supplement, but others should be approved under a new application. *Id.* at 3.

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Second, an application-based framework would create an easily administrable bright line rule based on a familiar standard, to the benefit of both CMS and manufacturers. A bright line rule would enable CMS to more readily identify relevant dosage forms and strengths for purposes of aggregating Medicare expenditures and applying the MFP.[24] And a bright line rule would enable manufacturers to more confidently track the seven- or eleven-year "qualifying single source drug" clock, and thereby make more informed decisions about research and development.

For these reasons, BIO strenuously disagrees with CMS's approach to identifying a qualifying single source drug by reference to common active moiety (drugs) or common active ingredient (biologics). Both law and policy dictate that a qualifying single source drug be identified by reference to its NDA or BLA.

Notably, it necessarily follows from the identification of a qualifying single source drugs by reference to its NDA or BLA that the dosage forms and strengths of such a drug (across which Medicare expenditures are aggregated and the MFP is applied) also must be identified by reference to the NDA or BLA of the drug. With respect to a qualifying single source drug, the statute requires CMS to aggregate Medicare expenditures "us[ing] data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug, such as an extended release formulation, and not based on the specific formulation or package size or package type of the drug."[25] Similarly, with respect to a qualifying single source drug that is a selected drug, the statute requires CMS to "establish[] . . . procedures to compute and apply the maximum fair prices across different strengths and dosage forms of [the] drug and not based on the specific formulation or package size or package type of such drug."[26] Accordingly, Medicare expenditures are to be aggregated, and the MFP is to be applied, across only dosage forms and strengths of the qualifying single source drug. As set forth above, a qualifying single source drug must be identified by reference to its NDA or BLA; it necessarily follows that the dosage forms and strengths of such a drug also must be identified by reference to the NDA or BLA of the drug.[27]

It is imperative that CMS immediately rescind the approach set forth in the Initial Guidance—under which Medicare expenditures are aggregated, and the MFP is applied, across dosage forms and

[24] *See* SSA §§ 1192(d)(3)(B), 1196(a)(2).
[25] *Id.* § 1192(d)(3)(B) (emphasis added).
[26] *Id.* § 1196(a)(2) (emphasis added).
[27] The references to "formulations" in the statutory text do not change the analysis. In context, such formulations are plainly limited to formulations of the dosage forms and strengths of the qualifying single source drug. *See, e.g.,* A. Scalia & B. Garner, *Reading law: The interpretation of Legal texts* 199, 203-132–33 (2012) ("[T]he verb to include introduces examples, not an exhaustive list."). We note that formulations of dosage forms and strengths may be approved under the same NDA or BLA. *See* FDA, Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees 3–4.

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strengths of products that share the same active moiety (drugs) or the same active ingredient (biologics)—and instead specify that, for purposes of aggregation of Medicare expenditures and application of the MFP, dosage forms and strengths are also identified by reference to the NDA or BLA of the qualifying single source drug, consistent with the requirements of the statute.[28]

C. Orphan drugs

BIO urges CMS to clarify the scope of the orphan drug exclusion in a manner that maximizes protection for orphan drugs.

A drug is categorically ineligible for selection for negotiation if "designated as [an orphan drug] for only one rare disease or condition . . . and . . . the only approved indication (or indications) is for such disease or condition."[29] It is imperative that CMS implement the orphan drug exclusion to be maximally protective of orphan drugs, in recognition of the unique need to maintain incentives for developing new therapies targeting rare diseases.

The Negotiation Program poses special risks to patient populations awaiting the development of new orphan drugs. By definition, orphan drugs target diseases affecting less than 200,000 people in the United States.[30] As such, such drugs are particularly susceptible to the chilling effect of factors that discourage research and development. On average, the development of a single drug takes anywhere from ten to fifteen years and costs upwards of $2.6 billion in research and development[31]—and the development of an orphan drug, often takes even longer and costs even more. Limited patient populations make it inherently more challenging for the developers of orphan drugs to recoup this investment, especially because orphan drug developers are overwhelmingly small emerging companies: Start-ups and emerging biotechnology companies are responsible for fully 85% of all orphan-designated products in development.[32]

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[28] Regardless of the "qualifying single source drug" definition adopted by the Agency, CMS must consistently apply such definition. As such, if CMS were to maintain that products that share the same active moiety (drugs) or the same active ingredient (biologics) are the same qualifying single source drug, BIO agrees that the market entry of a generic or biosimilar to any such product would disqualify all such products from treatment of a qualifying single source drug. *See* Initial Guidance at 10. Any other approach would be irreconcilable with CMS's stated "qualifying single source drug" definition. *See, e.g.*, *Nat'l Credit Union Admin. v. First Nat. Bank & Tr. Co.*, 522 U.S. 479, 501–02 (1998) (a basic canon of interpretation is that similar or identical language "be accorded a consistent meaning").

[29] SSA § 1192(e)(3)(A) (such drugs are categorically ineligible for selection for negotiation because they are excluded from the definition of "qualifying single source drug").

[30] *See* 21 C.F.R. § 316.10(d)(8)(ii).

[31] T. Sullivan, A Tough Road: Cost to Develop One New Drug Is $2.6 Billion, Policy & Med., https://www.policymed.com/2014/12/a-tough-road-cost-to-develop-one-new-drug-is-26-billion-approval-rate-for-drugs-entering-clinical-de.html (Mar. 21 2019).

[32] D. Thomas & C. Wessel, *2019 Emerging Therapeutic Company Trend Report, BIO Industry Analysis* 40 (2019), *available at* http://go.bio.org/rs/490-EHZ-999/images/BIO%202019%20Emerging%20Company%20Trend%20Report.pdf.

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As such, it is vitally important that CMS take special steps to protect development of and access to orphan drugs. The stakes could not be higher for patients. There are over 7,000 known rare diseases, and approximately thirty new ones are identified each year.[33] While each rare disease affects only a relatively small number of patients, collectively, over thirty million Americans are affected by a rare disease, with an estimated cost to society in excess of $1 trillion annually.[34] Further, 95% of rare diseases currently have no approved medical treatment.[35] According to a 2020 IQVIA/National Organization for Rare Diseases report examining trends in rare disease innovation, "there are [only] 447 drugs with orphan-only indications, with 104 drugs approved for two or more orphan indications."[36] As such, there is a pressing need to maintain strong incentives for continuing orphan drug development.

Research and development regarding the application of existing therapies to rare diseases is one way to chip away at this disparity. The orphan drug exclusion, however, discourages precisely such scientific discovery. Therefore, as the Agency "consider[s] whether there are additional actions CMS can take in its implementation of the Negotiation Program to best support orphan drug development,"[37] BIO urges the Agency to implement, at a minimum, the following recommendations to better support ongoing development of and access to drugs targeting patients living with rare diseases.

First, CMS should establish a process that enables manufacturers to submit evidence that an indication falls within an orphan drug designation to account for situations where CMS is unable to determine eligibility for the orphan drug exclusion based on a review of FDA's orphan drug databases.

As set forth above, the orphan drug exclusion is based on whether a drug has an orphan drug designation for a single rare disease, and whether its approved indications are for such rare disease.[38] In many cases, CMS will be able to readily determine whether a drug meets such

[33] BIO, Rare Diseases & Orphan Drugs, https://www.bio.org/policy/human-health/rare-diseases-orphan-drugs (last visited Feb. 28, 2023).
[34] S. Garrison, et al., *The Economic Burden of Rare Diseases: Quantifying the Sizeable Collective Burden and Offering Solutions*, Health Affairs Forefront, https://www.healthaffairs.org/do/10.1377/forefront.20220128.987667/ (Feb. 1, 2022).
[35] Nat'l Insts. of Health, *Delivering Hope for Rare Diseases* 1 (Jan. 2022), *available at* https://ncats.nih.gov/files/NCATS_RareDiseasesFactSheet.pdf.
[36] IQVIA, *Orphan Drugs in the United States* 7 (Dec. 2020), *available at* https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/orphan-drugs-in-the-united-states-rare-disease-innovation-and-cost-trends-through-2019/orphan-drugs-in-the-united-states.pdf.
[37] Initial Guidance at 11.
[38] SSA § 1192(e)(3)(A).

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criteria using publicly available information. This is because FDA maintains various databases containing relevant information.[39]

But there are situations where an approved indication falls within the scope of an orphan drug designation but there is no corresponding grant of orphan exclusivity.[40] In such situations, CMS cannot rely on FDA's databases, as the Agency states in the Initial Guidance it will do,[41] to accurately determine eligibility for the orphan drug exclusion—because those databases principally track orphan exclusivity, rather than orphan drug designation.[42]

To account for such situations, CMS should create a process that enables manufacturer to provide evidence that an indication falls within an orphan drug designation, where such fact is not ascertainable from FDA databases alone. Acceptable evidence should include written communications with FDA, whether pre- or post-approval. CMS should also establish this process as soon as possible, so that manufacturers can work with FDA and otherwise develop evidence that their drugs are eligible for the orphan drug exclusion, well in advance of the first selected drug publication date.

Second, CMS should confirm that it will determine eligibility for the orphan drug exclusion based on orphan drug designation *at the time of selection*.

Under FDA regulations, a manufacturer may voluntarily withdraw a requested or granted orphan drug designation at any time.[43] Where a manufacturer does so, the withdrawal is publicized, and any benefits associated with the designation cease.[44] Accordingly, when determining eligibility for the orphan drug exclusion, CMS should confirm that it will look only to orphan designation at the time of selection, and will not look to any prior designation that has been withdrawn. Doing so would help avoid improperly narrowing the universe of protected orphan drugs.

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[39] Such databases include FDA's orphan drug designation/exclusivity database, the drugs@FDA database, and the Approved Drug Products with Therapeutic Equivalence Evaluations publication (Orange Book).

[40] There are various circumstances where this can arise. For instance, it can occur in certain circumstances where an orphan drug is approved for the same indication as a previously approved drug, but is not clinically superior to the previously approved drug. In such a circumstances, although the indication falls within the scope of the orphan designation, it does not qualify for orphan exclusivity.

[41] Initial Guidance at 11.

[42] Orphan exclusivity is, in itself, irrelevant for purposes of the orphan drug exclusion. The orphan drug exclusion is unambiguously based on whether all indications of a drug with a single orphan drug designation fall within the scope of that designation. It is therefore immaterial whether the drug also has (or had) orphan exclusivity.

[43] 21 C.F.R. § 316.24(d).

[44] *Id.*

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Third, CMS should clarify that, where an orphan drug loses eligibility for the orphan drug exclusion, the seven- or eleven-year "qualified single source drug" clock runs from *the date on which the drug lost eligibility for the exclusion*.

Doing so would help maximize protection for orphan drugs. Absent such clarification, an orphan drug that loses eligibility for the orphan drug exclusion could be virtually immediately subject to selection for negotiation, simply because it was designated as an orphan drug for a second rare disease or an indication was approved for a second rare disease. CMS's implementation of the orphan drug exclusion would thereby disincentivize progress in rare disease drug development, which is often predicated upon identification of promising new uses of existing therapies. CMS should act to avoid such a result, as it would further disincentivize developers of orphan drugs from investing in treatments for a second rare disease.

Implementing the above recommendations is necessary to mitigate the risk that the Negotiation Program will deter the development of orphan drugs to treat those suffering from rare diseases. It is also fully consistent with long-standing Congressional policy favoring protection of orphan drugs. Such policy dates back to the early 1980s, when Congress enacted the Orphan Drug Act of 1983 to create various incentives to encourage and facilitate the development of new orphan drugs.[45] In keeping with Congress's long-held policy of protecting orphan drugs, CMS should make every effort to ensure that it does not hamper orphan drug innovation as it implements the Negotiation Program and its orphan drug exclusion.

D. Small biotech drugs

Under the IRA, a drug is exempt from negotiation for initial price applicability years 2026, 2027, and 2028 if spending on the medicine comprises: (1) a small percentage of Medicare program spending, and (2) a significant proportional share of a company's Medicare business. This is referred to as the Small Biotech Exception. This critical protection recognizes that small biotech manufacturers with a single product that represents the vast majority of their Medicare revenue will be disproportionately impacted by negotiation, which could have an immediate and tangible impact on the ability of such manufacturers to invest in future R&D – and in particular, in areas that predominantly affect the Medicare population.

CMS does not address how or when it will notify manufacturers regarding its determination of whether a drug, based on the information the manufacturer submits through the proposed ICR, qualifies for the Small Biotech Exception**. To that end, our comments that follow focus on ensuring predictability and**

[45] *See* Orphan Drug Act, Pub. L. No. 97-414, §§ 1, 2, 96 Stat. 2049, 2049–51 (1983), *as amended by* Pub. L. 98-551, 98 Stat. 2815, 2817 (1984).

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transparency for small biotech manufacturers that apply for the exception. This includes the following process attributes:

- Clear process (i.e., who submits, what to submit, when to submit) for applying for or recertifying a drug qualifies for the Small Biotech Exception.
- Appropriate and fair timelines to submit information to qualify.
- Consistency and clear criteria in evaluating submissions to qualify for the Small Biotech Exception.
- Proper and timely notification regarding qualification if the drug meets the Small Biotech Exception requirements.
- Proper and timely notification if the drug does NOT meet the Small Biotech Exception requirements, as well as a clear dispute process for appeal of such decision.
- Clarity regarding the form and manner that CMS will use to notify manufacturers if they meet – or do not meet – the criteria for the Small Biotech Exception.

Submissions for Initial Price Applicability Year 2026. CMS has indicated that the current Small Biotech Exception ICR is focused only on initial price applicability year 2026. However, as discussed further below, given that the agency has not made publicly available the data on which it will rely with regard to total expenditures for the purpose of determining eligibility for the Small Biotech Exception under section 1192 (d)(2,) or whether a drug meets the test of a high spend drug under section 1192 (d)(1), it is impossible for small biotech manufacturers to make a reasonable inference regarding whether a submission is warranted in the current or future years on the basis of the requisite statutory thresholds. We recommend that any company that believes it qualifies for the Small Biotech Exception under section 1192 (d)(2) should be able to apply and be approved for this exception this year regardless of whether the drug meets the test of a high spend drug under section 1192 (d)(1). This will provide important certainty and predictability for small biotech manufacturers. Such certainty is critical as most small biotech manufacturers have only one or a limited number of products on the market. We also believe the statute contemplates such an approach, as the exception in section 1192 (d)(2)(A) refers to a "qualifying single source drug" that meets either the test in section 1192 (d)(2)(A)(i) or section 1192 (d)(2)(A)(ii), and these tests refer to Medicare expenditures in 2021, and the data for any small biotech company is readily available to CMS. To provide additional predictability and mitigate uncertainty for small biotech manufacturers, CMS should also clearly articulate the specific criteria manufacturers should consider in determining whether to apply for the Small Biotech Exception for initial price applicability year 2026.

Clarity on Process and CMS Response to Small Biotech Manufacturer. CMS should specify not only the timeline for when the submission of information by the small biotech manufacturer is due, but also the timeline for CMS review and response to the manufacturer, in situations where CMS grants the

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exception as well as situations where CMS does not. To promote certainty for small biotech manufacturers, CMS should commit to responding to each manufacturer as far in advance of September 1, 2023, as possible.

- *Clear Timelines.* We suggest the following as a timeline that would allow for appropriate transparency, clarity, and completion of the process in advance of the September 1, 2023, publication of drugs selected for negotiation:
    - Submission by small biotech manufacturers due June 10, 2023;
    - CMS response to small biotech company (affirmative or negative) due by June 30, 2023;
    - Small biotech company response to negative determination by July 20, 2023;
    - Final CMS response to small biotech company by August 10, 2023.

- *Clarity on Data Source for 2021 Drug Spending and Availability of Data for Manufacturers.* CMS should clarify what data source it will use for identifying 2021 total expenditures for the qualifying single source drug, as the agency has stated that the drug dashboard data published at *cms.gov* is not being used for the IRA negotiation provisions; we also understand CMS is considering use of Prescription Drug Event (PDE) data. We recommend that CMS provide the data it will be using for 2021 to manufacturers so that this data can be validated by manufacturers that apply for (or will apply for) the Small Biotech Exception.

- *CMS Response and Justification for Decision.* CMS should provide clarity on the form and content of its expected response and notification to small biotech manufacturers applying for the exception, specifically whether the response will be by letter, email, or other form of official communication. Further, if CMS determines that it does not agree that a small biotech drug qualifies for the exception, CMS's response should outline in sufficient detail how such a determination was made, including on which expenditure data the agency relied and other information, as relevant, that led to a negative determination. Further, CMS should indicate if the rationale for the denial is restricted to initial price applicability year 2026 or all years for which the Small Biotech Exception applies.

- *Dispute Resolution.* CMS should provide a dispute resolution process where the manufacturer can respond to and appeal a negative determination by CMS. Specifically, the small biotech manufacturer should have the opportunity to provide additional data or information to the agency to support its application for the Small Biotech Exception.

- *Flexibility.* Given that this is a new program and process, and that only a limited number of small biotech manufacturers will be providing submissions to CMS, we recommend that the agency allow for a flexible approach. For example, if CMS determines that information submitted by the

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small biotech manufacturer is incomplete or unclear, we urge CMS to engage in a dialogue with the manufacturer to resolve any outstanding issues to complete their submission. Further, for the first year of the program, we encourage CMS to allow a small biotech manufacturer to submit information after the information submission deadline, such as in good faith circumstances where a small biotech manufacturer may later realize that it should qualify for the exception.

- *One-time Qualification.* We request that manufacturers should not need to reapply in subsequent years if a drug has previously received the Small Biotech Exception and there is no material change in the manufacturer's circumstances. Manufacturers could submit an attestation that nothing in their application has materially changed from the prior year and if there has been a material change the manufacturer could submit an updated form.

- *Clear Definition of "Acquired."* We recommend CMS include a definition for what it means to be "acquired" pursuant to section 1192(d)(2)(B)(ii). CMS should consider defining an acquisition as the transfer of substantially all assets of the manufacturer. Further, CMS should specify whether the acquiring manufacturer meeting the definition of a specified manufacturer will be determined at the time of acquisition. If the acquisition results in a change in eligibility for the small biotech exemption, an updated form should be submitted.

- *Confidentiality of Proprietary Information, Publication of Drugs Qualifying for Small Biotech Exception.* As with all other aspects of the data submitted under provisions of the IRA, CMS must fully protect the confidentiality of all proprietary information submitted in relation to this ICR. At the same time, CMS should outline its approach for sharing with the public information regarding the small biotech drugs the agency determines qualify for the exception. Further, BIO recommends that CMS publish a summary list of the small biotech drugs and manufacturers that qualified. Such information will be important for understanding the impact of this IRA provision and provide further certainty to small biotech manufacturers. We believe that more detail on

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how or why a specific manufacturer's drug qualified as a small biotech drug should only be released if that manufacturer chooses to do so.

II. Selection, and Delayed Selection, for Negotiation

A. Background

For each IPAY, the statute directs CMS to publish a list of the drugs that have been selected for negotiation (under statutorily specified parameters) by February 1 of the year that is two years before such IPAY.[46]

The statute provides for a delay in the selection of a biologic for negotiation where, among other things, CMS finds that a biosimilar is highly likely to come to market within two years of what otherwise would be the selected drug publication date.[47] A first year of delay is granted if the following criteria are met:

- The biologic otherwise would be an extended-monopoly drug;[48]
- The biosimilar manufacturer requests the delay before what would otherwise be the selected drug publication date;[49]
- The biosimilar manufacturer submits specified information and documents;[50]
- CMS finds that the biosimilar is highly likely to be licensed and market within two years of what otherwise would be the selected drug publication date;[51] and
- Certain disqualifying circumstances are not present.[52]

A second year of delay is granted if the following criteria are met:

- The biologic otherwise would remain an extended-monopoly drug;[53]
- The biosimilar manufacturer requests the delay before the date that is one year after what would otherwise be the selected drug publication date;[54] and
- CMS finds that the biosimilar is highly likely to be licensed and marketed within two years of what otherwise would be the selected drug publication date and that, based on clear and

[46] SSA §§ 1191(b)(3), 1192(a); *see also id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).
[47] *Id.* § 1192(f).
[48] *Id.* § 1192(f)(1)(A); *see also id.* § 1194(c)(4) (defining "extended-monopoly drug").
[49] *Id.* § 1192(f)(1)(B)(i)(I).
[50] *Id.* § 1192(f)(1)(B)(ii).
[51] *Id.* § 1192(f)(2)(A).
[52] *Id.* § 1192(f)(2)(D)(iii), (iv).
[53] *Id.* § 1192(f)(2)(D)(ii).
[54] *Id.* § 1192(f)(1)(B)(i)(II).

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convincing evidence, the biosimilar manufacturer has made substantial progress toward licensure and marketing;[55] and

- Certain disqualifying circumstances are not present.[56]

Where a second year of delay is not granted or the biosimilar does not come to market within two years of what otherwise would be the selected drug publication date, the biologic is selected for negotiation, and the biologic manufacturer must pay a specified rebate.[57]

B. Pre-selection process

Well in advance of the selected drug publication date, CMS should notify each manufacturer of each drug that it intends to select for negotiation and afford each such manufacturer a reasonable opportunity to dispute the propriety of each such intended selection.

The process for selecting a drug for negotiation is complex. Eligibility for selection is based on multiple factors, including whether a sufficient number of years have elapsed since approval or licensure;[58] whether a generic or biosimilar has come to market;[59] whether the drug is eligible for the orphan drug exclusion;[60] whether the drug is a plasma-derived product;[61] whether the drug is a small biotech drug;[62] whether Medicare expenditures are sufficiently low to disqualify the drug from selection;[63] and whether Medicare expenditures are sufficiently high to qualify the drug for selection.[64]

The intricate nature of the selection process presents an inherent risk of a selection error. Notably, if a selection error were identified after the selected drug publication date, CMS would de-select the erroneously selected drug but could not select a substitute. By statute, for a given IPAY, all drugs must be selected by February 1 of the year that is two years before the IPAY.[65]

CMS can readily mitigate this concern by adopting a process for soliciting feedback from manufacturers of potential selected drugs before the selected drug publication date. Specifically, CMS should provide notice to each such manufacturer at least thirty days in advance of the selected drug publication date.

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[55] *Id.* § 1192(f)(2)(B)(i), (iii).
[56] *Id.* § 1192(f)(2)(D)(iii), (iv).
[57] *Id.* § 1192(f)(2)(B)(ii), (C).
[58] *Id.* § 1192(e)(1).
[59] *Id.*
[60] *Id.* § 1192(e)(3)(A).
[61] *Id.* § 1192(e)(3)(C).
[62] *Id.* § 1192(d)(2).
[63] *Id.* § 1192(e)(3)(B).
[64] *Id.* § 1192(d)(1).
[65] *Id.* §§ 1192(e), 1192(a); *see also id.* § 1191(d)(1) (September 1, 2023, for IPAY 2026).

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CMS should then afford the manufacturer at least fourteen days to identify to the Agency any basis on which the manufacturer believes the drug is not, in fact, eligible for selection. Such a pre-selection process would serve an important role in identifying selection errors and further the Agency's interests in transparency, efficiency, and informed decision-making.

In addition to providing advance notice to each manufacturer of a drug that the Agency intends to select, CMS should provide advance notice to each manufacturer of at least each of the next five drugs that would be selected if one or more drugs that the Agency intends to select were found to be ineligible for selection. Doing so would promote efficiency by giving each such manufacturer the same opportunity to engage with the Agency regarding potential selection errors. And doing so would impose no additional burden on the Agency because CMS is already required to identify the top fifty qualifying single source drugs by Part D expenditures and, starting with IPAY 2028, the top fifty qualifying single source drugs by Part B expenditures.[66]

In addition, in advance of the deadline by which a biosimilar manufacturer must request a delay in the selection of a reference biologic for negotiation, CMS should enable such biosimilar manufacturer to ascertain whether the reference biologic is among the drugs that the Agency intends to select (or one of at least the next five drugs in line for selection).

As set forth above, a biosimilar manufacturer may request a delay in the selection of a reference biologic for negotiation.[67] By statute, such a request must be submitted before the selected drug publication date.[68] This requirement results in a fundamental timing conundrum: A biosimilar manufacturer will not know whether it should request a delay until after the deadline for requesting the delays has passed.

CMS tacitly acknowledges this timing conundrum in the Initial Guidance but fails to meaningfully address it. The Initial Guidance provides only that a biosimilar manufacturer that "think[s]" that a reference biologic "may" be selected for negotiation should submit a delay request.[69] This approach is inadequate. Requiring a biosimilar manufacturer to guess whether to submit a delay request is deeply inefficient and unreasonable; just as "[i]t is one thing to expect regulated parties to conform their conduct to an agency's [actions] once the agency announces them; it is quite another to require regulated parties to divine the agency's [actions] in advance."[70]

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[66] *See id.* § 1192(d)(1).
[67] *Id.* § 1192(f).
[68] *Id.* § 1192(f)(1)(B)(i).
[69] Initial Guidance at 16.
[70] *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 158–59 (2012).

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To make the delay request provision meaningful, it is essential that CMS instead create a way for a biosimilar manufacturer, with appropriate confidentiality safeguards, to ascertain whether a reference biologic is likely to be selected before the delay request submission deadline. CMS should enable a biosimilar manufacturer to inquire with the Agency starting at least thirty days in advance of such deadline.

C. Delayed selection of a biologic for negotiation on account of anticipated biosimilar market entry

As set forth below, BIO makes a number of recommendations to enhance the implementation of the process by which a biosimilar manufacturers may request a delay in the selection of a reference product for negotiation.

As set forth above, the statute directs CMS to delay the selection of a biologic for negotiation under specified circumstances.[71] BIO makes the following recommendations to enhance the implementation of the delay process:

First, it is vital that CMS afford a biosimilar manufacturer a *meaningful* opportunity to request a delay, reset the delay request submission deadline closer to the selected drug publication date and permit broad supplementation of a timely request.

If CMS does not adopt these recommendations, it will undermine the fidelity of the information on which it relies in making a "high likelihood" determination—and indeed Congress's objective in providing for a delay request.

With respect to the timing of a delay request, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023.[72] CMS will then provide a fillable template to complete and access to a Box folder within five business days, i.e., by May 17, 2023.[73] The manufacturer must then upload a completed templated and all supporting documentation by May 22, 2023—only three business days later, yet over three months in advance of the selected drug publication date.[74] There is no justification for such an extraordinarily and needlessly truncated window of time in which to submit a multifactorial request—a concern that is only compounded by CMS's policy of automatically denying an

[71] SSA § 1192(f).
[72] Initial Guidance at 21.
[73] *Id*.
[74] *Id*.

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incomplete request.[75] Indeed, such timing constraint works to defeat the Congressional objective in providing for a delay request: By effectively eliminating the additional runway for a biosimilar competitor to come to market, it acts as a barrier to the biosimilar competition that Congress sought to nurture. It is imperative that CMS afford a biosimilar manufacturer a meaningful opportunity to request a delay.

In addition, to ensure that CMS adjudicates a delay request based on the most mature information possible, CMS should (1) set the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permit broad supplementation of a timely request with late-breaking information or otherwise for good cause. As noted above, under the Initial Guidance, a biosimilar manufacturer must give notice of its intent to submit a delay request by May 10, 2023—over three months in advance of the selected drug publication date.[76] And CMS will permit supplementation by the biosimilar manufacturer, beyond supplementation requested by the Agency, only with respect to whether the BLA has been accepted or approved by FDA.[77]

Information bearing on the expected timing of licensure and marketing often rapidly changes. The expected timing of market entry can fluctuate based on a range of factors, including FDA communications regarding the BLA and changes to the manufacturer's production or distribution arrangements. In order for CMS to make an informed determination regarding eligibility for delayed selection, it is vitally important that the Agency rely on all of the most recent available information that bears on the likelihood of market entry within the requisite time period.

An accurate "high likelihood" determination also reduces administrative burden. If CMS makes an erroneous determination based on outdated or incomplete information, the Agency will be required to administer the payment of a rebate by the reference biologic manufacturer. Such needless inefficiency can be avoided by enabling the Agency to rely on the most recent available information by (1) setting the delay request submission deadline as close as reasonably possible to the selected drug publication date and (2) permitting broad supplementation of a timely request with late-breaking information or otherwise for good cause.

Second, CMS should provide notice of its delay request determination in advance of the selected drug publication date and establish a dispute resolution process.

[75] *Id*. at 22.
[76] *Id.* at 21.
[77] *Id.* at 23.

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Under the Initial Guidance, CMS will not inform a biosimilar manufacturer of an unsuccessful delay request until after the selected drug publication date.[78] This effectively means that the biosimilar manufacturer will have no opportunity to dispute the determination.

The Agency instead should provide notice of an unsuccessful delay request in advance of the selected drug publication date and establish a process by which the biosimilar manufacturer can dispute an erroneous determination. BIO recommends that CMS provide such notice at least fourteen days in advance of the selected drug publication date and afford the biosimilar manufacturer at least seven days to dispute the determination.

Third, CMS should accept and consider all information that the biosimilar manufacturer determines relevant to determining eligibility for delayed selection.[79]

As noted above, there are countless factors that can affect the expected timing of licensure and approval. It follows that CMS should not artificially limit the information that it considers in determining eligibility for delayed selection. Accordingly, it is vital that CMS enable the biosimilar manufacturer—the party closest to the information—to submit all information that it determines relevant to the delay request.[80]

There is clear statutory authority to enable the biosimilar manufacturer to submit such information. The statute provides that the biosimilar manufacturer must submit "information and documents necessary for [CMS] to make [the delayed selection determination], as specified by [CMS] . . . ."[81] In addition, the statute provides that, after CMS has reviewed the delay request, the biosimilar manufacturer must submit "any additional information and documents requested by [CMS] necessary to make [the delayed selection determination]."[82]

CMS therefore has broad discretion in specifying what the biosimilar manufacturer must submit in support of the delay request. The Agency should exercise such discretion and request that the manufacturer submit all relevant information. Doing so would help ensure that CMS has the most pertinent information before it, as the biosimilar manufacturer is the entity best situated to identify the information that bears on the delay request.

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[78] *Id.* at 24.
[79] *See* SSA § 1192(f)(1)(B)(ii)(I)(aa) ("information and documents necessary for the Secretary to make determinations under this subsection, as specified by the Secretary"), (II) ("additional information and documents requested by the Secretary necessary to make determinations under this subsection").
[80] In the Initial Guidance, CMS enables the submission of only the statutory minimum information. Initial Guidance at 22.
[81] SSA § 1192(f)(1)(B)(ii)(II). The statute goes on to specify that such information "includ[es]" the information specified in section 1192(f)(1)(B)(ii)(III). *Id.*
[82] *Id.* § 1192(f)(1)(B)(ii)(II).

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Notably, CMS also has clear legal authority to consider all such information in making a "high likelihood" determination.

Section 1192(f)(3) sets forth a set of circumstances under which CMS must find a high likelihood of timely market entry—based on a limited set of enumerated information and documents, including information and documents described in section 1192(f)(1)(B)(ii)(III) (subclause (III)).[83] Critically, section 1192(f)(3) cannot be interpreted to set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

The broader structure of section 1192(f) makes clear that Congress intended that the full range of relevant information and documents be considered by CMS, not only the limited set of information and documents enumerated in section 1192(f)(3). This is because section 1192(f)(1)(B)(ii)(I)(aa) (subclause (I)(aa)) clearly requires the biosimilar manufacturer to submit information and documents necessary to rendering the "high likelihood" determination—"includ[ing]" (but not limited to) the information and documents described in subclause (III).

The necessary implication is that there are information and documents beyond the information and documents described in subclause (III)—which are also "necessary" to rendering the "high likelihood" determination. While the information and documents described in subclause (III) are accounted for in section 1192(f)(3), the remaining information and documents described in subclause (I)(aa) are not—despite being "necessary" to rendering the "high likelihood" determination. Thus, if section 1192(f)(3) were the only set of circumstances under which CMS may find a high likelihood of timely market entry, the language in subclause (I)(aa) requiring broad submission of pertinent information and documents beyond those in subclause (III) would be rendered a nullity.[84] Because the information and documents described in subclause (I)(aa) serve no other statutory purpose, the only way to give meaning to the entirety of subclause (I)(aa) is to assign it its most natural meaning: Information and documents described in subclause (I)(aa) are "necessary" to rendering the "high likelihood" determination and, thus, CMS may consider all such information and documents submitted in rendering such determination. Accordingly, section 1192(f)(3) does not set forth the set forth the only set of circumstances under which CMS may find a high likelihood of timely market entry.

There is every reason to think that Congress intended for CMS to consider all relevant evidence in rendering the "high likelihood" determination. Any other interpretation of the statute would

[83] *Id.* § 1192(f)(3).
[84] *See Duncan v. Walker*, 533 U.S. 167, 175 (2001) (a statute is not to be interpreted in a manner that renders any provision a nullity or otherwise meaningless).

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yield an absurd result. Through subclause (I)(aa), Congress clearly granted CMS broad discretion to identify and collect information and documents "necessary" to rendering the determination. If CMS were to refuse to consider such information, it would be tantamount to the Agency acknowledging that it is rendering the determination without considering information and documents that the Agency itself has concluded is essential to doing so. It is hard to imagine more arbitrary and capricious governmental decision-making.[85] Accordingly, CMS should request all information that a biosimilar manufacturer concludes supports a "high likelihood" determination and consider all such information in rendering such determination.

Fourth, we appreciate CMS's confirmation that an agreement between a biosimilar manufacturer and a reference biologic manufacturer that permits the biosimilar manufacturer to market the biosimilar is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay. But we ask for clarification on the circumstances under which CMS will find a disqualifying agreement to exist.

The statute provides that a delay request may not be granted where, based on specified information,[86] a biosimilar manufacturer and a reference biologic manufacturer have entered into an agreement that incentivizes (or requires) the biosimilar manufacturer to request a delay.[87] In the Initial Guidance, CMS correctly acknowledges that an agreement between a biosimilar manufacturer and a reference biologic manufacturer "that permits the Biosimilar Manufacturer to [timely] market the Biosimilar in one or more dosage form(s), strength(s), and indication(s)" not only is not necessarily an agreement that incentivizes the biosimilar manufacturer to request a delay but indeed can be a form of clear and convincing evidence of a high likelihood of timely market entry.[88] It would be contrary to the statute for CMS to suggest otherwise. This is because the statute clearly directs CMS to consider agreements between the biosimilar manufacturer and the reference biologic manufacturer in rendering the delayed selection determination.[89] It would nullify this statutory instruction if the mere existence of an agreement between the biosimilar manufacturer and the reference biologic manufacturer were automatically disqualifying. It is well understood that a statute should not be interpreted in a manner that renders text meaningless or otherwise nugatory.[90]

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[85] *See* 5 U.S.C. § 706(2)(A).
[86] SSA § 1192(f)(1)(B)(ii)(I)(bb) ("all agreements related to the biosimilar biological product filed with the Federal Trade Commission or the [Department of Justice] pursuant to subsections (a) and (c) of section 1112 of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003," which include agreements between "brand name drug companies" and "generic drug applicants").
[87] *Id.* § 1192(f)(2)(D)(iv).
[88] Initial Guidance at 19.
[89] SSA § 1192(f)(1)(B)(ii)(I)(bb), (2)(B)(i)(II), (3)(B).
[90] *United States v. DBB, Inc.*, 180 F.3d 1277, 1285 (11th Cir. 1999) ("A statute should be 'interpreted so that no words shall be discarded as meaningless, redundant, or mere surplusage.'") (internal citations omitted).

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BIO, however, asks CMS to clarify the circumstances under which the Agency will find a disqualifying agreement to exist. In the Initial Guidance, CMS states only that an agreement may not "impos[e] improper constraints on the Biosimilar Manufacturer."[91] Yet, despite the absence of meaningful guidance regarding such constraints, CMS will require a biosimilar manufacturer requesting a delay to certify that it has not entered into a disqualifying agreement,[92] on pain of potential "liability, including under the False Claims Act."[93] To promote market certainty by enabling manufacturers to more confidently make more informed decisions about the arrangements into which they enter, it is imperative that CMS clarify what constitutes an agreement that incentivizes a biosimilar manufacturer to request a delay.

III. Negotiation Process

A. Background

The statute requires CMS to "develop and use a consistent methodology and process" to negotiate the MFP.[94] In addition, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY.[95] CMS must make a written initial offer by June 1, which must include a concise justification that considers certain statutorily enumerated negotiation factors.[96] Within thirty days of receipt, the manufacturer must accept the initial offer or make a written counteroffer, which must include a justification that considers the same statutorily enumerated negotiation factors.[97] CMS must respond in writing to any counteroffer,[98] and the negotiation period must end by November 1.[99]

[91] Initial Guidance at 19.
[92] *Id.* at 77.
[93] *Id.* at 80.
[94] SSA § 1194(b)(1). The renegotiation process must be consistent with the negotiation process to the extent practicable. *Id.* § 1194(f)(1), (4).
[95] *Id.* §§ 1194(b)(2)(A), (e)(1), 1194(a)(4); *see also Id.* § 1191(d)(5)(A) (October 2, 2023, for IPAY 2026).
[96] *Id.* § 1194(b)(2)(B); *see also Id.* § 1191(d)(5)(B) (February 1. 2024, for IPAY 2026).
[97] *Id.* § 1194(b)(2)(C).
[98] *Id.* § 1194(b)(2)(D).
[99] *Id.* § 1194(b)(2)(E); *see also Id.* § 1191(d)(5)(C) (August 1, 2024, for IPAY 2026).

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B. Negotiation process

BIO asks CMS to adopt its recommendations to improve the proposed negotiation process.

As noted above, the statute mandates that CMS "develop and use a consistent methodology and process" for MFP negotiation.[100] Thus, Congress intended for the negotiation process to be transparent to and predictable for all parties. Although no two negotiations will ever be identical—because the circumstances of each selected drug are unique—all negotiations should be subject to a clear and reasonable framework. A consistent process not only is statutorily required but also helps to ensure that CMS complies with its obligation to treat similarly situated entities in a similar manner, absent a reasoned basis for distinction.[101]

The Initial Guidance proposes that, only where CMS rejects a counteroffer, the Agency will extend an invitation for a negotiation meeting to take place within thirty days of receipt of such counteroffer.[102] CMS would hold a maximum of three such meetings: an initial meeting and up to one additional meeting at the request of either CMS of the manufacturer.[103] The Initial Guidance also proposes to allow the parties to discuss new information during such meetings.[104]

With respect to justifying of an initial offer, the Initial Guidance only recites the statutory requirement of a concise justification based on the statutorily enumerated negotiation factors.[105] The Initial Guidance is silent as to any justification of a response to a counteroffer.

BIO makes the following recommendations to improve the proposed negotiation process:

> **First, CMS should further enable a negotiation process that allows for meaningful engagement and dialogue between CMS and manufacturers**. BIO appreciates that CMS's recognition that real dialogue (as opposed to a paper-based process) is essential to fulfilling Congress's intent in establishing a "Negotiation" Program with a mandated process "for negotiations,"[106] which necessarily contemplates meaningful engagement between the Agency and the manufacturer on the unique circumstances presented by each selected drug.[107]

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[100] *Id.* § 1194(b)(1).
[101] *See Bracco Diagnostics*, 963 F. Supp. at 27–28.
[102] Initial Guidance at 55.
[103] *Id.* at 55–56.
[104] *Id.* at 56.
[105] *Id.* at 54.
[106] SSA § 1194(b)(1).
[107] *See Wheeler v. St. Joseph Hosp.*, 133 Cal. Rptr. 775, 790 (Ct. App. 1976) (differentiating between "negotiated contracts" and contracts of adhesion).

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BIO, however, is concerned that the agency is arbitrarily limiting such engagement to (1) the period after the rejection of a counteroffer and (2) a maximum of three meetings. There is no logical reason for such limitations, as (1) such engagement can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, and (2) the parties may agree that one or more additional meetings would be helpful and productive in setting the MFP. Accordingly, BIO encourages CMS to revise its proposed negotiation process to (1) enable real dialogue between the parties throughout the negotiation process and (2) specify that, where CMS rejects a counteroffer, additional meetings, beyond those proposed by CMS, may be held without limit where both parties agree to them. We note that such modifications to the negotiation process would be readily manageable given the limited number of drugs subject to such negotiation in any given year.[108]

Second, the manufacturer should more generally be permitted to supplement its timely submission where a post-submission development arises or there otherwise is good cause. As set forth above, the statute requires the manufacturer to submit specified information by March 1 of the year that is two years before the applicable IPAY. Inevitably, there will be situations where information relevant to the negotiation arises after the submission deadline has passed. Such late-breaking developments will often be completely unforeseeable at the time of submission but highly relevant to the setting of the MFP. The potential scenarios are virtually limitless: For example, new therapeutic alternatives may come to market; production costs may shift due to ingredient shortages or supply chain issues; or new comparative effectiveness studies may become available.

BIO acknowledges CMS's recognition that it should not blind itself to highly pertinent new information, simply because the submission deadline has passed. But the Agency proposes to limit the presentation of such information to the negotiation meetings during the period after the rejection of a counteroffer. Because such information can equally inform an initial offer, potentially sparing the parties the need to consider a counteroffer, the Agency should more generally permit the manufacturer to supplement its timely submission wherever there is good cause to do so, including when new information relevant to the negotiation process becomes available after the submission deadline.

Permitting supplemental submissions is well warranted. Under the statute, manufacturers are given only one month to prepare a voluminous submission of complex information, including information regarding Non-Federal average manufacturer price (Non-FAMP); research and

[108] *See* SSA § 1192(a).

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development costs; production and distribution costs; federal financial support for discovery and development; pending and approved patent applications, FDA exclusivities, NDAs or BLAs and approvals thereof, market data; and revenue and sales volume data.[109] In some cases, requested data may also not exist in a format required by CMS, such that the manufacturer will need to painstakingly convert raw data from multiple sources into such a format. Manufacturers will assuredly work with utmost diligence to comply with CMS's submission requirements. Still, they may need the flexibility of a supplement to their timely submission for legitimate reasons.

Ultimately, more generally permitting the manufacturer to supplement its timely submission where there is good cause would help ensure that the MFP is set based on the best available information.

Third, CMS should provide a *meaningful* justification of its initial offer and its response to any counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set.

As noted above, Congress intended for the MFP to be set via "negotiation," meaning a bilateral "discussion or process of treaty" between the parties "aimed at reaching an agreement about a particular issue."[110] As with any good faith negotiation, open dialogue will be vital to the success of the MFP negotiation. To this end, BIO asks CMS to specify that its initial offers and its responses to any counteroffers include *meaningful* explanations of how the Agency arrived at the offer or response, including by explaining how the offer or response is supported by the statutorily enumerated negotiation factors and any other information upon which the Agency relied, and how the Agency considered and weighted such factors and information.

As noted above, in the Initial Guidance, CMS states only that the Agency's justification for an initial offer will be "based on" its analysis of statutorily enumerated negotiation factors, but it does not commit to disclosing the details of such analysis.[111] The Agency does not commit to providing any justification for a response to a counteroffer or an explanation of how it arrived at such response.[112]

[109] *Id.* §§ 1193(a)(4), 1194(e)(1).
[110] Oxford English Dictionary, Definition of Negotiation, https://www.oed.com/view/Entry/125879?redirectedFrom=negotiation#eid (last visited Mar. 2, 2023).
[111] Initial Guidance at 54.
[112] *See id.* at 56–57.

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Fully disclosing the bases of both offers and responses to counteroffers would facilitate a more robust—and ultimately more effective—negotiation process. By providing the manufacturer with a meaningful justification for an offer or response, CMS would provide greater opportunity for bilateral dialogue, which would result in more informed and targeted discussions.

BIO also asks CMS to commit to responding to any counteroffer within thirty days. We further ask CMS to commit to affording the manufacturer at least thirty days to comment on the response and considering any such comment before the MFP is set.

This basic procedural protection is essential. Not only would it be consistent with the Agency's stated interest in "prioritiz[ing] transparency and robust engagement,"[113] but it would also result in more informed and accurate decision-making. It would help prevent the MFP from being set based on an error, a misunderstanding, or a gap in information.

There is ample time in the negotiation schedule for such procedural protection. By statute, an initial offer is made by June 1 (February 1, 2024, for IPAY 2026).[114] A counteroffer is made within thirty days of receipt.[115] Even if CMS were to wait until June 1 (February 1, 2024, for IPAY 2026) to make the initial offer, and even if the manufacturer were to wait until the thirtieth day after receipt make the counteroffer, there would still be four months remaining in the negotiation schedule (five months for IPAY 2026). Thus, there would be ample time for the recommended additional process.

C. Confidential commercial information

BIO acknowledges CMS's stated commitment to confidentiality, but recommends that CMS establish more fulsome safeguards to ensure that the Agency is adequately protecting the confidentiality of all proprietary information submitted to CMS as part of the negotiation process. In addition, BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers.

The statute imposes a clear confidentiality requirement: "Information submitted to . . . [CMS] . . . by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by . . . [CMS]) shall be used only by . . . [CMS] or disclosed to and used by the Comptroller General of the United States for purposes of carrying out [the Negotiation Program]."[116] Congress imposed this

[113] CMS, Medicare Drug Price Negotiation Program: Next Steps in Implementation for Initial Price Applicability Year 2026 at 1 (Jan. 1, 2023), *available at* https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-next-steps-implementation-2026.pdf.
[114] SSA § 1191(d)(5)(A).
[115] *Id.* § 1194(b)(2)(B).
[116] *Id.* § 1193(c).

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confidentiality requirement for good reason. The statute mandates that manufacturers of selected drugs submit highly sensitive information as part of the negotiation process—including, among other things, information regarding Non-FAMP, research and development costs, production and distribution costs, and revenue and sales volume data.[117] It would be deeply disruptive to commercial markets if such proprietary information were disclosed or used in violation of the confidentiality requirement. Indeed, the Initial Guidance acknowledges the "highly sensitive" nature of information to be submitted under the program.[118] In principle, BIO is therefore encouraged that CMS states that it "intends to implement a confidentiality policy that is consistent with existing requirements for protecting proprietary information, such as Exemption 4 of [the Freedom of Information Act (FOIA)]."[119] That said, there is a pressing need for more detailed specification as to how the Agency will safeguard confidential commercial information to ensure that the statute's robust confidentiality requirement is fully honored.

BIO therefore asks CMS to more fully specify the controls and safeguards that it will implement. We urge CMS to ensure that such controls and safeguards maximize the protection of confidential commercial information to be submitted under the program. This would be fully consistent with the approach taken in other areas of federal law and policy, which have long given special consideration to such highly sensitive information. For nearly forty years, the Supreme Court has made clear that commercial trade secrets are a "property right [] protected by the Taking Clause of the Fifth Amendment."[120] Likewise, Congress has repeatedly made clear its expectation that commercially sensitive information be appropriately safeguarded. For example, even beyond FOIA's long-standing protection of "trade secrets and commercial or financial information that is obtained from a person and is privileged or confidential,"[121] the Defend Trade Secrets Act prohibits the "misappropriation" of trade secrets through public disclosure and established a private cause of action to enable affected parties to sanction such misappropriation.[122]

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

> **First, CMS should confirm that, in "implement[ing] a confidentiality policy that is consistent with existing requirements for protecting proprietary information,"[123] it will ensure protections comparable to, not only those under FOIA, but also those under government price reporting law and policy.**

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[117] *Id.* §§ 1193(a)(4), 1194(e)(1).
[118] Initial Guidance at 29.
[119] *Id.*
[120] *Ruckelshaus v. Monsanto Co.*, 467 U.S. 986, 1004 (1984).
[121] 5 U.S.C § 552(b)(4); 45 C.F.R. § 5.31(d).
[122] 18 U.S.C. § 1839(5)(B)(ii)(II).
[123] Initial Guidance at 29.

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We appreciate CMS's confirmation that the protections under FOIA, including the prohibition on disclosure of information designated as confidential without providing a pre-disclosure notification and an opportunity to raise objections to disclosure,[124] will apply to information to be submitted under the program.[125] We seek confirmation that the protections under government price reporting law and policy will also apply.

In developing the Negotiation Program, Congress did not intend to disrupt the confidentiality requirements under other federal law and policy.[126] CMS's confidentiality policy should thus maintain the confidentiality of information protected against disclosure under all other federal law and policy. For example, under MDRP, "information disclosed by manufacturers . . . under [MDRP] . . . is confidential and shall not be disclosed by [CMS] . . . in a form which discloses the identity of a specific manufacturer . . . [or] prices charged for drugs by such manufacturer . . . ."[127] Similarly, Medicare Act provides that "[Average Sales Price (ASP)] information disclosed by manufacturers . . . is confidential and shall not be disclosed by [CMS] in a form which discloses the identity of a specific manufacturer . . . or prices charged for drugs or biologicals by such manufacturer . . . ."[128] Likewise, the 340B Drug Pricing Program (340B Program) generally prohibits disclosures of information submitted by manufacturers under the program.[129] Where confidential commercial information is protected against disclosure under these or any other federal programs, CMS should safeguard such information against disclosure to at least the same extent.

Second, CMS should implement robust storage and access controls and safeguards to protect the confidentiality of sensitive information. Confidentiality requirements are only as meaningful as the data privacy and security protections that are implemented to safeguard sensitive information against inadvertent or malicious[130] improper disclosure. Accordingly, CMS should implement robust systems and protocols, including by ensuring that all proprietary information stored in the Health Plan Management System (HPMS) and in electronic

[124] *See* 45 C.F.R. §§ 5.41, 5.42.
[125] Initial Guidance at 29.
[126] *See Nat'l Ass'n of Home Builders v. Defs. of Wildlife*, 551 U.S. 644, 662 2d 467 (2007) ("[R]epeals by implication are not favored" and will not be presumed unless the "intention of the legislature to repeal [is] clear and manifest.").
[127] SSA § 1927(b)(3)(D) (subject to certain limited exceptions).
[128] *Id.* § 1847A(f)(2)(D) (subject to certain limited exceptions).
[129] Health Res. & Servs. Admin., General Instructions for Completing the Pharmaceutical Pricing Agreement 7 (2019), *available at* www.hrsa.gov/sites/default/files/hrsa/opa/pharmaceutical-pricing-agreement-example.pdf.
[130] Malicious third-party cyber activities have increasingly targeted the federal government—in, part, because its databases are repositories of significant amounts of sensitive information. *Cf.* David E. Sanger, *Russian Hackers Broke into Federal Agencies, U.S. Officials Suspect*, N.Y. Times, https://www.nytimes.com/2020/12/13/us/politics/russian-hackers-us-government-treasury-commerce.html (last updated May 10, 2021).

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communications with the Agency is secure and accessible only to CMS staff and only where there is a legitimate programmatic need for access to such information.

In doing so, CMS should look to the safeguards it has already establish under MDRP. Under MDRP, CMS has implemented a system with numerous privacy and security protections to safeguard sensitive product and pricing data submitted by manufacturers. For example, the online interface allows a manufacturer to view its pricing data, such as its Baseline Average Manufacturer Price (AMP) data, while disallowing states, which do not have a programmatic need to view such information, from doing likewise.[131] CMS should ensure that similar controls are in place with respect to HPMS, given CMS's intent to transition most information submissions to that system.

CMS should also specify how it will maintain the confidentiality of the subset of information that is required to be submitted via e-mail or Box. With respect to e-mail, CMS should explain, among other things, how it will enforce access security controls. With regard to Box (a third-party commercial platform), BIO asks CMS to specify how submitted information will be kept confidential, including as against misuse by Box personnel.

Third, CMS should establish a process to enable manufacturers to review a draft of the explanation of the MFP in advance of its publication and raise concerns about disclosure of confidential information. By statute, CMS is required to publish an explanation of the MFP.[132] Such publication inherently poses heightened risk of disclosure of confidential commercial information. BIO appreciates that CMS intends to make only high-level comments regarding submitted data and refrain from sharing proprietary information.[133] But this is insufficient to safeguard against inadvertent disclosure of confidential commercial information. Accordingly, BIO asks that the manufacturer be given an opportunity to review the intended explanation in advance of publication, as well as an opportunity to raise concerns. Such precaution is well warranted here, given Congress's special emphasis on the need for safeguards with respect to the public explanation of the MFP, as evidenced by its specific cross-reference to the statute's confidentiality requirement.[134]

BIO opposes CMS's proposed imposition of overly broad confidentiality obligations on manufacturers. BIO urges CMS to eliminate the proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all

[131] CMS, *Medicaid Drug Programs User Manual* 1 (Nov. 3, 2021).
[132] SSA § 1195(a)(2).
[133] Initial Guidance at 29.
[134] SSA § 1195(a)(2); *see also id.* § 1193(c).

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information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Like CMS, manufacturers are responsible for maintaining records associated with material decisions and must do so to maintain proper and adequate lines of supervision and oversight by boards, shareholders, and other stakeholders. Manufacturers must therefore be permitted to maintain (in a confidential format) reasonable records associated with the negotiation process to meet their oversight obligations, just as CMS will be maintaining its own records from the negotiation process.

Further, basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. As CMS knows, the statute contemplates penalties of up to $1 million per day for failing to submit required information. CMS's Initial Guidance further specifies that the Agency will consider a manufacturer that knowingly submits false information to have violated this provision. Especially given the vast magnitude of such penalties, it is imperative that manufacturers be permitted to maintain complete records of all information they believe may be relevant to defending against the erroneous imposition of sanctions.

It would be troubling in the extreme if manufacturers were required by CMS to destroy the very records that could one day be needed to defend against penalties that could reach hundreds of millions of dollars. "[T]he essence of due process is fundamental fairness," and little could be more fundamentally unfair than mandating destruction of the very records needed to verify an entity's innocence as against erroneous enforcement.[135]

Moreover, BIO takes issue with the more specific blanket prohibition on manufacturers from disclosing or otherwise publicizing information "in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers…". As with the broader records destruction provisions discussed above, this prohibition amounts to CMS putting its thumb on the scale of transparency as the only entity involved in the negotiation program who can control and confirm information flows. This one-sided information control heightens the ultimate public complaint that the entirety of the "negotiation" process is anything but. Rather, optically – and in practice – it appears CMS is proposing to control the entirety of the negotiation process, and to stifle any outside public discussion of the negotiation process itself. BIO disagrees with this approach and recommends CMS abandon it.

Further, the blanket "gag" sought in the proposed guidance raises several practical and Constitutional concerns. From a broader regulatory standpoint, certain regulatory agencies (*e.g.* The Securities and Exchange Commission) might well have conflicting standards for materiality determinations in disclosures made by publicly traded companies. We would argue that the exclusion in the guidance

[135] *Evans v. Wilkerson*, 605 F.2d 369, 371 (7th Cir. 1979).

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from the disclosure prohibition based on state and federal law might not go far enough in covering certain regulatory obligations – both at the federal and state level. Particularly when considered in context with the records destruction obligations imbued in the guidance as well.

What is more, CMS appears to be making a more general affront to the protected speech of affected manufacturers. As has been reaffirmed many times before, prior restraints on speech are presumptively unconstitutional.[136] The government faces a heavy burden in showing a compelling interest in keeping negotiation discussions private, and we fail to see a legitimate reason why the government's interests are so advanced by muzzling private companies in the context of Medicare price negotiation discussions.[137] In fact, in this instance, any potential disclosure by a manufacturer would likely relate to truthful information that is, at a minimum, of significance to at least a portion of the public involved in the transaction of health insurance and health consumption. As such, we recommend CMS abandon these burdensome and unnecessary confidentiality and anti-disclosure provisions.

D. Special considerations in setting the MFP

It is vital that, in setting the MFP, CMS impose on itself bright-line limitations that mitigate the negative effects of the IRA and the MFP on patient access and on therapeutic innovation. BIO strongly urges CMS to adopt the following limitations.

BIO asks CMS to commit to a policy where it will not set the MFP below a price shown to imperil patient access (or otherwise below the MFP ceiling).

It is basic economics that centralized price-setting risks curtailing access to the supply of medicines.[138] If the government mandates a price too far below the price that would have been set by the free market, there will be an inevitable and profound mismatch between demand and supply.[139]

BIO urges CMS, in carrying out the Negotiation Program, to be attuned to the risk to patient access if the MFP is set unduly low. The stakes are too high for CMS not to give due weight to such risk. The implication of a supply-demand mismatch is not limited to some economist's spreadsheet. Rather, it

[136] *See, e.g., Near* v. *Minnesota* 283 U.S. 697 (1931).
[137] As has been reaffirmed in many instances by the US Supreme Court, the government must articulate a compelling government need for the negotiation to remain out of the public discourse and must simultaneously introduce a narrowly tailored method for so restricting this discussion. In the context of this guidance, we see no such articulation of either a compelling need nor a narrow restriction. In fact, we see just the opposite. *See, e.g., New York Times Co.* v. *United States,* 403 U.S. 713 (1971).
[138] S. Atlas, *How to Reduce Prescription Drug Prices: First, Do No Harm*, 117 Modern Med. 14, 14 (2020).
[139] Rent control is the classic Economics 101 illustration: Price controls on rental stock result in undersupply; the result is a net societal loss of utility relative to the pareto optimal price. *See, e.g.*, E. Glaser & E. Luttmer, *The Misallocation of Housing Under Rent Control*, 93 Am. Econ. Rev. 1027, 1027 (2003).

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could mean the difference between millions of patients having access to life-saving medicines and empty shelves at the pharmacy counter. Indeed, the House Committee on Ways and Means has estimated that loss of innovation due to price controls could result in as many as "42 million patients without the medicine they need."[140]

The risk to longer-term innovation and development of new medicines is even more profound. One recent study by the University of Chicago concluded that the "mid-range effect" of price controls is 254 fewer new drug approvals; the researchers conservatively estimated that the loss in life from the price controls accordingly is twenty times larger than our country's losses from the COVID-19 pandemic.[141] Another study of the European experience found that a "10% drop in the price of medicines in price-controlled [European Union] markets was associated with . . . an 8% increase in the delay of access to medicines."[142] Still other studies have demonstrated that government price-setting is associated with dramatic declines in early research, which, of course, is the fundamental precursor to a robust and growing pipeline of new therapies targeting areas of unmet medical need.[143]

Therefore, CMS should commit to a policy under which it will not set the MFP below a price shown to further imperil patient access (or otherwise below the MFP ceiling). This approach would help strike an equitable balance, giving weight to the objective of reducing prices today while also mitigating the risk that price controls will significantly imperil the drug supply or further curtail the development of the transformative medicines of tomorrow.

BIO also asks CMS to commit to setting the MFP at the MFP ceiling where failing to do so would further curtail therapeutic innovation.

It is vital that the Negotiation Program strike an appropriate balance such that blunt reductions in Medicare expenditures do not come at the expense of ongoing innovation that yields new and potentially life-saving medicines. Accordingly, BIO urges CMS to commit to setting the MFP at the MFP ceiling where doing otherwise would imperil therapeutic innovation, including in the following circumstances (not exhaustive):

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[140] U.S. House Comm. on Ways & Means, Analysis: Americans Don't Support Surrendering Innovation, https://waysandmeans.house.gov/analysis-americans-dont-support-surrendering-innovation-for-democrats-drug-price-controls/ (Aug. 4, 2022).

[141] *See* T. Phillipson & T. Durie, The Evidence Base on the Impact of Price Controls on Medical Innovation 1 (2021) (loss in life estimate was over a ten-year time period), *available at* https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

[142] D. Schulthess & H. Bowen, *The Historical Impact of Price Controls on the Biopharma Industry*, Vital Transformations (Nov. 22, 2021).

[143] *See* T. Abbott & J. Vernon, *The Cost of US Pharmaceutical Price Reductions: A Financial Simulation Model of R&D Decisions*, 28 Managerial & Decision Econ. 293 (2007).

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First, for a drug (small molecule), the MFP should not be set below the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

To be selected for negotiation, biologics (large molecules) must be at least eleven years post-licensure, while drugs (small molecules) must be at least seven years post-approval.[144] On account of the approximately two-year time lag between selection for negotiation and application of the MFP, an MFP cannot apply to a biologic until at least approximately thirteen years post-licensure; in contrast, an MFP cannot apply to a drug until at least approximately nine years post-approval. To help preserve small molecule innovation in parity with large molecule innovation, we ask that, for a small molecule, CMS set the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Studies show that most products (whether small or large molecules) achieve modest levels of annual sales in their first five years on the market.[145] Thus, manufacturers may seek the economic benefit of an additional four-year shelter from selection for negotiation by focusing research and development on biologics instead of drugs.

Thus, we ask that CMS act to better balance the incentives regarding small molecule drug and biologic development by setting the MFP for a small molecule drug at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the drug is thirteen years post-approval.

Second, the MFP should not be set below the MFP ceiling during any year of the price applicability period into which patent protection extends.

CMS must consider a number of factors in determining the MFP for a selected drug, including "[d]ata on pending and approved patent applications."[146] We ask CMS to ascertain whether, based on information submitted by the manufacturer, the selected drug will have any remaining patent protection at the start of the price applicability period and, if so, set the MFP at the MFP ceiling price for any year during such period into which such patent protection extends.

[144] SSA § 1192(e)(1).

[145] QuintilesIMS Inst., *Lifetime Trends in Biopharmaceutical Innovation: Recent Evidence and Implications*, at 2 (Jan. 2017).

[146] SSA § 1194(e)(1)(D).

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The statute permits a drug to be subject to an MFP nine years post-approval and a biologic to be subject to an MFP thirteen years post-licensure.[147] By the time the price applicability period for a selected drug begins, the product's regulatory exclusivity period likely will have expired—but not necessarily its patent protection period.[148] In other words, given that a patent protection period can extend beyond a regulatory exclusivity period, it may very well be the case that there will be remaining patent protection for a selected drug that extends into the price applicability period.

In the Initial Guidance, CMS proposes that, if a selected drug "has patents and exclusivities that will last a number of years," CMS may adjust the "preliminary price" downward.[149] This is the opposite of what the policy should be. A selected drug's ongoing patent protection supports a higher "preliminary price"—and, indeed, an MFP equal to the MFP ceiling. This is key to supporting pharmaceutical and biotechnology innovation in developing drugs and biologics that treat serious diseases.

It is a long and expensive process to bring a chemical or biological product from research and development to market, and many candidates do not make it through the process. To encourage innovation by rewarding manufacturers for their research and development investments and efforts, the federal government awards pharmaceutical and biotechnology companies with patent protection for a specified period of time. The patent protection period affords a manufacturer the opportunity to recover its research and development costs—not only for the drug for which the patent was awarded but also for other research and development investments that the manufacturer made. To support continued innovation, CMS should honor any remaining patent protection for a selected drug by specifying that the MFP will be set at the MFP ceiling during any year of the price applicability period into which such patent protection extends.

Third, the MFP should be set at the MFP ceiling until at least the first year during the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval.

Innovation should not end with the approval of a first indication. Rather, finding novel uses for existing therapies is "essential for maximizing medicines' therapeutic utility."[150] Developers of

[147] *Id.* § 1192(e)(1).

[148] *See* FDA, Frequently Asked Questions on Patents and Exclusivity, available here (last accessed Mar. 2023).

[149] Initial Guidance at 53.

[150] B. Sahragardjoonegani et al., Repurposing existing drugs for new uses: A cohort study of the frequency of FDA-granted new indication exclusivities since 1997, 14 J. of Pharmaceutical Policy & Practice 1 (2021).

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drugs and biologics therefore devote countless hours and untold capital to research and development of new indications, thereby expanding treatments to additional disease states and patient populations.[151]

In recent years, new indications have spurred vital medical breakthroughs across countless critical medical conditions. For example, new indications have been vital "to increase the portfolio of available effective cancer chemotherapeutic agents for patients."[152] Similarly, the repurposing of existing therapies has played a critical role in meeting the otherwise unmet needs of patients with rare medical conditions.[153]

The seven- and eleven-year selection clocks work to extinguish such innovation by actively disincentivizing a manufacturer from making the considerable investment necessary to obtain approval of a new indication, given that such indication would run on the same selection clock. CMS must act to mitigate this concern by committing to setting the MFP at the MFP ceiling until at least the first year of the price applicability period that starts after the date on which the most recently approved indication is thirteen years post-approval. Such limitation on the setting of the MFP would provide greater certainty to manufacturers as they consider ongoing investment in research and development of new indications. This could avoid wholesale extinguishment of therapeutic innovation, to the detriment of patients with serious unmet medical needs, on account of the seven- and eleven-year selection clocks.

Fourth, the MFP should not be set below the MFP ceiling for vaccines recommended by the Advisory Committee on Immunization Practices (ACIP) at the Centers for Disease Control (CDC). Vaccination is often cited among the 10 greatest public health achievements of the century. In addition to their societal benefit, vaccines deliver significant benefit to individuals throughout their lifetime and allow older individuals to remain healthier and productive in their later years of life. The importance of vaccines was recognized in the IRA, which eliminated cost sharing for vaccines in Medicare Part D, building on the precedent in Medicare Part B where there was no cost sharing for vaccines. Because of the high value that vaccines confer not only to Medicare beneficiaries but to society as a whole, the MFP for vaccines recommended by the ACIP should not be set below the MPF ceiling.

[151] *See id*. at 1–2 (noting the significant time and cost associated with obtaining approval of a new indication).
[152] S. Islam, et al., Repurposing existing therapeutics, its importance in oncology drug development: Kinases as a potential target, 88 Br. J. Clin. Pharmacol. 64 (2021).
[153] *See* P. Ayyar et al., Repurposing – second life for drugs, 69 Pharmacia 51, 52 (2022).

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IV. Negotiation Factors

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

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

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

The statute also directs CMS not to use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

A. Evidence on therapeutic alternatives and unmet need

CMS should emphasize factors related to clinical value and unmet need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

In developing a starting point for the initial offer, CMS proposes to utilize the net price for identified therapeutic alternatives and then adjust this starting point based on the review of the clinical evidence to develop a "preliminary price." CMS will then consider the manufacturer specific data under section 1194(e)(2) and may adjust the preliminary price upward or downward. When there is no therapeutic alternative CMS would adjust the starting point based on how the selected drug fills an unmet medical need.

The proposed approach outlined by CMS is vague, and CMS's intent is unclear. We strongly support an approach that emphasizes factors related to clinical benefit and unmet medical need and de-emphasizes manufacturer specific data elements such as cost of production and research and development costs – CMS should clarify how it will weight these factors in that regard. CMS should consider and prioritize high quality, robust real-world evidence (RWE), evidence provided by clinicians with the necessary expertise, as well as evidence submitted by manufacturers – who have a vast depth and breadth of

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clinical and scientific expertise regarding their marketed therapies. CMS should also focus on patient-centered outcomes and the broader societal benefit conferred by a therapy. Further, providing higher relative MFPs to products that have advanced patient care and undress unmet medical need will help maintain investment in assets and clinical programs that show scientific promise. At the same time, it is critical that CMS is transparent in its approach in determining therapeutic alternatives to selected drugs and provides a strong justification that the identified therapeutic alternatives are appropriate and are primarily driven by clinical guidelines and patient need versus cost.

It is essential that CMS clarify how it will evaluate the evidence it receives from different stakeholders and how such evidence will be considered in identifying therapeutic alternatives and setting the MFP.

CMS says it would adjust the preliminary price based on the totality of the relevant information and evidence submitted and gathered through the agency's analysis based on the clinical benefit the selected drug provides compared to its identified therapeutic alternatives. We support an approach that considers a wide range of high quality, robust evidence, including RWE. Further, information submitted by manufacturers should be considered a high priority in CMS's review as manufacturers have deep and unique expertise in their therapeutic areas of focus.

CMS should be transparent and provide sufficient detail regarding its framework for how different evidence was used to inform the identification of therapeutic alternatives for a selected drug, as well as the establishment of the preliminary price as well as the initial offer and response to any counteroffer, including what evidence was most impactful in CMS' analysis and why. CMS' review of the evidence should be patient-centered and have a focus on health equity and reducing disparities. To that end, we strongly support CMS's confirmation that evidence that uses discriminatory approaches such as QALYs will not be considered. We also note that other measures that have been often promoted as alternatives to QALYs – such as the Equal Value of Life Years Gained (evLYG) – are also problematic as they limit the value of interventions that both extend life and improve the quality of life – and CMS should similarly reject them. In reviewing the evidence CMS should recognize both the current and future value of therapies and remain flexible to keep pace with innovations in science and technology. Further, evidence on a therapy should be viewed in the context of its benefits to the Medicare program, as well as the overall health care system.

We recommend that CMS provide manufacturers with robust detail regarding its analysis of evidence throughout the negotiation process and provide manufacturers with opportunities for discussion and dialogue, including before CMS's initial offer in February 2024 and in its identification of therapeutic alternatives that will be used in setting the MFO. CMS should also provide a line of sight into its assessment of the evidence for the broader stakeholder community, so as to ensure appropriate

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transparency and accountability not just to manufacturers but to Medicare beneficiaries and to providers and other key stakeholders.

We are concerned that CMS's proposed definition of unmet medical need is too limiting; the agency should use a more robust definition. We recommend that CMS look to the FDA's definition outlined in its "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics.[154] Under the FDA guidance, "An unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs)."

B. Submission of Information on Negotiation Factors Related to Therapeutic Alternatives and Unmet Need (Section 1194(e)(2))

CMS's approach and processes for collecting information on the negotiation factors related to therapeutic alternatives and unmet medical need should ensure that a robust, comprehensive set of information submitted by manufacturers– with any necessary supplemental material – will be accepted and considered by CMS.

The negotiation guidance references the Negotiation Data Elements ICR, which describes how CMS intends to collect data on the negotiation factors. We are concerned that CMS's approach may be too limiting in practice and will not allow for a robust submission of information - including any supplementary material – by manufacturers. We will be providing more detailed comments on the ICR, but note Questions 40 through 43, which collect information on prescribing data, therapeutic impact and comparative effectiveness, comparative effectiveness in specific populations, and unmet medical needs. The data fields are limited to 1,000-3,000 words, which is insufficient in length. Further, the data fields do not seem to contemplate submission of complementary information, such as charts and tables. We strongly recommend that CMS reconsider its approach and permit manufacturers to submit any information they determine relevant to the negotiation process (including information not related to the negotiation factors enumerated in the statute). Further, CMS should be required to consider all such information, not just the negotiation factors in sections 1194(e)(1) and 1194(e)(2).

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

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C. Submission of Manufacturer-Specific Data (Section 1194(e)(1))

We understand that the IRA requires CMS to consider factors under both section 1194(e)(1) and section 1194(e)(2). **However, as noted above, we believe CMS should de-emphasize factors the manufacturer-specific data in section 1194(e)(1) and focus on the factors that matter most to patients – those that are focused on clinical value and unmet need. In addition, to address issues that we highlight below, we recommend that, in lieu of the proposed standardized definitions, CMS allow manufacturers to use reasonable assumptions (with accompanying justifications) regarding the information they submit on the manufacturer-specific data.**

There are important considerations that will make it difficult – if not impossible – for CMS to standardize the definitions for the manufacturer-specific factors. For example, regarding research and development costs, a key issue for CMS to consider is that companies, and investors, invest in research and development for "programs" in a specific disease area, not simply discrete drugs. A program can have many drugs or biologicals at different stages of development each with multiple indications, and all which would factor into the research and development costs for an FDA-approved or licensed therapy. This can include thousands and sometimes millions of compounds that could be screened early in the research and development process, with a success rate of less than 12%.[155]

Further, it can be misleading to approximate "value" using research and development costs. Not all companies conduct research and development in the same manner. Some smaller companies might undertake single-therapeutic, high-risk approaches to developing a compound, while many others, often bigger companies, conduct research using the "programs," as noted. These differences in the way research and development can be conducted could disadvantage companies in negotiation if manufacturer-specific data is too heavily relied upon for "value."

Looking at research and development costs in the post-market setting can also be misleading because of ongoing costs that are difficult to quantify. For example, the FDA requires post-market safety monitoring, these costs can also be augmented if a manufacturer must utilize FDA-mandated risk evaluation and mitigation strategies (REMS), something to which not every manufacturer is subjected. Another example is costly post-market clinical trials that can take years.

We also are concerned with CMS's proposed requirement to collect information that is not collected today – once example is net revenue "without patient assistance programs." It is unclear why CMS would be collecting data in this manner and the underlying implication of patient assistance programs on price.

[155] Biopharmaceutical Research and Development: The Process Behind the Medicines, PhRMA. 2015. Accessed: 03/28/2023. http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf

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In other areas, the definitions CMS proposes are unclear, which will make it difficult for manufacturers to comply with submission requirements. For example, regarding data on approved and pending patents, clarifications are required to better define the patents and pending patent applications that must be disclosed. More precision is required where CMS is asking for patents "relating" or "linked to" the selected drug, as it is unclear what CMS means – related or linked how? In this respect, we also note that "patent" and "patent application" are well-understood terms of art that don't require further definition in the CMS guidance. For example, the CMS guidance definition of a "pending patent application" specifies any patent application "for which a patent number has not been issued." This definition would plainly include applications that are not, in fact, pending because they have been abandoned. An "approved patent application" presumably means a patent application that has received a notice of allowance, meaning that it is still a pending patent application (and not a "patent") that does not require a special definition. And a "patent" comes into existence not on the date a patent application is "approved," but on the date a patent is issued, and the official patent grant is transmitted. We recommend deleting the special definitions of "pending patent application," "approved patent application," and "expired patent," and to change the operative language as suggested in our proposed edits below.[156]

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

- *CMS considers patents relevant to this data to include:*
  - *all patent applications pending in the USPTO, international patent applications filed under the Patent Cooperation Treaty that designate the United States, and all U.S. patents, that are owned by, licensed to, or controlled ~~pending and approved patent applications, including expired and non-expired approved patents, submitted, sponsored, licensed, and/or acquired~~ by the Primary Manufacturer ~~relating to the~~, and that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug as of September 1, 2023;*
  - *U.S. patents ~~linked to~~ that claim the selected drug, a constituent part of the selected drug, or an approved method of using the selected drug where the Primary Manufacturer is not listed as the assignee/applicant but with respect to which the manufacturer has enforcement rights (for example, for a joint venture product); and any patent that is with respect to the selected drug included in a list published under*

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

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section 351(k)(9) of the Public Health Service Act or section §505(j)(7) of the Federal Food, Drug, and Cosmetic Act, ~~patent applications, pending and approved~~, for which a claim of patent infringement could reasonably be, or has been, asserted against a person engaged in the unlicensed manufacture, use, or sale of the selected drug ~~in any form~~.

More fundamentally, CMS states it will consider the length of available patents and exclusivities and, if such patents and exclusivities will last for a number of years, the Agency may consider reducing the preliminary price downward. BIO strongly opposes such an approach. Rather, remaining patents and exclusivities should only be used to justify an *increase* in the preliminary price.

Regarding data on prior federal financial support in discovery and development, important contextual information should be considered by CMS. The biopharmaceutical industry's role in the U.S. research ecosystem is to undertake the clinical research and development required to advance basic science research by entities such as the National Institutes of Health (NIH) into safe and effective treatments available to patients. In 2018, the biopharmaceutical industry invested $102 billion in R&D, most of which was focused on clinical research. Meanwhile, the entire NIH budget in 2018 was $35.4 billion, only 8% of which was focused directly on clinical research.

Of note, of the 23,230 NIH grants in the year 2000 that were linked by NIH supported patents to 41 investigational drugs, only 18 had gained FDA approval by 2020. In fact, total private investment for these 18 approved medicines exceeded NIH funding by substantial orders of magnitude: $44.2 billion in private investment compared to $670 million in NIH. These findings are consistent with scholarship describing the complementary roles of public and private R&D funding, and the significant long-term investments shouldered by industry with no guarantee of approval. In fact, just 7.9% of medicines in clinical development are ultimately approved by the FDA.[157]

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

[157] Clinical Development Success Rates and Contributing Factors 2011-2020. Available at bio.org.

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V. MFP Ceiling

A. Background

The calculation of the MFP ceiling, which represents the maximum possible MFP, is the lowest of three amounts:

(1) the "applicable percent" of the Average Non-FAMP for 2021 (or, if there is such Non-FAMP, the Average Non-FAMP for the first full year following market entry), as increased by a Consumer Price Index for All Urban Consumers (CPI-U) factor;[158]

(2) the "applicable percent" of the Average Non-FAMP for the year before the year of the selected drug publication date (except for IPAY 2026);[159] or

(3) (a) for a Part D drug, the sum of each "plan specific enrollment weighted amount" for each prescription drug plan (PDP) or Medicare Advantage prescription drug (MA-PD) plan;[160] or

(b) for a Part B drug, the Part B payment amount for the year before the year of the selected drug publication date.[161]

The "applicable percent" is 75 percent for "short-monopoly drugs,"[162] 65 percent for "extended-monopoly drugs,"[163] and forty percent for "long-monopoly drugs."[164]

B. Average Non-FAMP

BIO recommends that, in defining Average Non-FAMP, CMS abandon its proposal to create a new price point calculated based on the four quarters of a calendar year, and instead simply adopt the existing annual Non-FAMP, calculated based on the four quarters of a federal fiscal year, under the Veterans Health Care Act of 1992 (VHCA).

As set forth above, Average Non-FAMP is calculated as part of determining the MFP ceiling.[165] Average Non-FAMP is a statutory term of art meaning "the average of the non-Federal average manufacturer

[158] SSA § 1194(c)(1)(A), (C). The CPI-U adjustment applies from September 2021 (or December of the first full year following market entry) to September of the year before the year of the selected drug publication date.
[159] *Id.*
[160] *Id.* § 1194(c)(1)A, (B)(i), (2).
[161] *Id.* § 1194(c)(1)(A), (B)(ii).
[162] *Id.* § 1194(c)(3)(A) (defining "short monopoly drug" as a selected drug that is not an "extended-monopoly drug" or "long-monopoly drug").
[163] *Id.* § 1194(c)(3)(B); *see also id.* § 1194(c)(4) (defining "extended monopoly-drug").
[164] *Id.* § 1194(c)(3)(C); *see also id.* § 1194(c)(5) (defining "long-monopoly drug").
[165] *Id.* § 1194(c)(1)(A), (C).

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price (as defined in section 8126(h)(5) of title 38, United States Code) for the 4 calendar quarters of the year involved."[166]

The statute 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), i.e., the VHCA. As such, the statute effectively instructs CMS to calculate Average Non-FAMP by reference to how annual Non-FAMP is calculated under the VHCA.

The VHCA requires manufacturers to calculate and report quarterly Non-FAMPs and an annual Non-FAMP—but does not require manufacturers to calculate and report an "average" Non-FAMP based on the four quarters of a calendar year. Rather, the annual Non-FAMP is calculated based on the four quarters of a federal fiscal year—which runs from October 1 through September 30.[167]

As such, the annual Non-FAMP is a stand-alone weighted average calculation based on data from the fourth quarter of a calendar year through the third quarter of the subsequent calendar year (i.e., the four quarters of a federal fiscal year).[168] The most coherent policy would be for CMS to adopt the same approach to calculating Average Non-FAMP for a year under the Negotiation Program. Given that the statute expressly cross-references the VHCA in the course of defining Average Non-FAMP, there is every reason to think that Congress wanted CMS to maximize alignment as between Average Non-FAMP and the annual Non-FAMP under the VHCA, rather than creating an entirely new price point.

In the Initial Guidance, however, CMS does not propose to borrow the established VHCA framework. Rather, CMS proposes to calculate Average Non-FAMP by reference to the four quarter of a calendar year.[169] This approach is inefficient and unnecessarily burdensome for both CMS and manufacturers. Under the proposal, the Agency will be obligated to develop, implement, and oversee a completely new process to facilitate collection of new pricing data, as the Agency cannot benefit from the efficiencies of the well-established process that VA has already put into place—because the VHCA approach is, as noted above, tied to a federal fiscal year, rather than a calendar year. By contrast, if the Agency instead were to borrow the existing VHCA framework, Average Non-FAMP would be equated with a price point that already exists, and all stakeholders would benefit from the resulting efficiencies.

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[166] *Id.* § 1194(c)(6).

[167] For example, the data used to calculate the annual Non-FAMP for 2021 cover the period from October 1, 2020, through September 30, 2021.

[168] The annual and quarter 3 Non-FAMPs submitted to the Department of Veterans Affairs (VA) are used to calculate the Federal Ceiling Price (FCP), which caps pricing under VA Federal Supply Schedule contracts. Manufacturers are required to submit quarters 1, 3, and 4 Non-FAMPs, too, but these price points have no impact on the price paid by the federal government. While the data used to calculate these quarterly Non-FAMPs are incorporated into the four quarters of data used to calculate the annual Non-FAMP, these quarterly Non-FAMPs themselves are not used to calculate the annual Non-FAMP.

[169] Initial Guidance at 42–44.

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If CMS does not reverse course, BIO agrees that CMS's framework should be based on a weighted average.[170]

A weighted average is consistent with the VHCA framework expressly cross-referenced in the statutory definition of Average Non-FAMP. A such, a weighted average better aligns to Congress's intent.

More importantly, use of a weighted average will objectively enhance accuracy because it will account for differences in volume across quarters and therefore create the most accurate picture of average wholesaler pricing. Such enhanced accuracy is why Congress has consistently required the use of weighted averages across the various federal pricing programs associated with federal health care programs: VHCA (Non-FAMP), Medicaid (AMP), and Medicare (ASP) all use weighted averages, not simple averages.

Congress has consistently required the use of weighted averages because simple averages are less accurate. Simple averages result in over-valuation of sales in quarters with lower sales volumes, and under-valuation of sales in quarters with higher sales volumes. As such, it is critically important that CMS use a weighted average to ensure more accurate calculations of Average Non-FAMP, and we concur with CMS's proposal to do so.

The Agency should establish an exceptions process to account for restatements and anomalies.

An exceptions process is vital. There will inevitably be situations where Average Non-FAMP will need to be restated in light of data errors or other issues identified after the fact or where an unusual circumstance will result in an anomalous Average Non-FAMP.

- **Non-FAMP restatements**. CMS must consider how it will address situations in which a Non-FAMP that is used for an MFP calculation is restated by the manufacturer and approved by VA. VA has long recognized the need for manufacturers to be able to restate a Non-FAMP where the reported Non-FAMP is determined to be inaccurate (e.g., sales data flaws, data system problems). The VA experience has demonstrated that restatements are not uncommon, with adjustments of contract pricing facilitated based on restated Non-FAMPs and FCPs. The Agency must expressly account for the need for such restatements—but the Initial Guidance does not do so.

[170] *Id.* at 43.

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- **Non-FAMP anomalies**. The VA's experience reveals a variety of circumstances where an anomalous Non-FAMP can arise due to a misalignment of sales dollars and units. This can occur due to lagged sales, market shortages, or various other factors. VA has developed various exceptions and workarounds for calculating FCPs when there are Non-FAMP anomalies. It is vital that CMS develop its own processes for addressing anomalous Average Non-FAMPs. Any approach adopted by CMS needs to be flexible to account for the wide range of circumstances that can result in an anomalous Average Non-FAMP.[171] But the Initial Guidance is silent on any such flexibilities.

BIO encourages CMS to adopt an exceptions process to account for Average Non-FAMP restatements and anomalies. In doing so, CMS should clarify how such process affects the MFP ceiling and, ultimately, the MFP.

C. Extended- and long-monopoly drugs

CMS should clarify whether the time period for determining whether a selected drug is an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

As set forth above, there are three options for setting the MFP ceiling. Two of these options look to the "applicable percent" of the applicable Average Non-FAMP.[172] By statute, the "applicable percent" varies based on whether the drug is a short-, extended-, or long-monopoly drug.[173]

With limited exceptions, extended monopoly drugs are, "with respect to an initial price applicability year, selected drug[s] for which at least 12 years, but fewer than 16 years, have elapsed since the date of approval . . . or . . . licensure,"[174] and long-monopoly drug are, "with respect to an initial price applicability year, selected drug[s] for which at least 16 years have elapsed since the date of approval . . . or licensure."[175] Short-monopoly drugs are all other selected drugs.[176]

Notably, the statute is silent as to the date to which the twelve- or sixteen-period that defines an extended- or long-monopoly drug runs. In the Initial Guidance, CMS takes inconsistent positions. On the one hand, CMS states that, for IPAY 2026, a delay request may be submitted where a reference

[171] For example, in certain cases, it may be prudent for CMS to account for an Average Non-FAMP anomaly by looking to the prior year's figures; in other cases (e.g., a new product), this may not be possible.
[172] SSA § 1194(c)(1).
[173] *Id.* § 1194(c)(3).
[174] *Id.* § 1194(c)(4)(A).
[175] *Id.* § 1194(c)(5)(A).
[176] *Id.* § 1194(c)(3)(A).

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biologic will have been "licensed for between 12 and 16 years prior to the start of the initial price applicability year on January 1, 2026."[177] On the other hand, in "Figure 2: Monopoly Types and Applicable Percentage for Initial Price Applicability Year 2026,"CMS conveys that, for IPAY 2026, it will count the 16-year period that defines a long-monopoly drug to September 1, 2023, i.e., the selected drug publication date for IPAY 2026.[178] In other words, CMS is inconsistent as to whether the twelve- or sixteen-year period that defines an extended- or long-monopoly drug runs to the start of the applicable IPAY, or to the applicable selected drug publication date.

BIO asks CMS to clarify its intended interpretation in light of the conflicting language in the Initial Guidance.

D. MFP ceiling for Part D drugs

BIO disagrees with CMS's intended approach for calculating the MFP ceiling option specific to Part D drugs. CMS must calculate the MFP ceiling under such option exclusive of manufacturer price concessions unless they are passed through at the point of sale, consistent with CMS's long-standing policy governing the Part D negotiated price.

As set forth above, one of the three options for determining the MFP ceiling with respect to a Part D drug is the sum of each "plan specific enrollment weighted amount" for each PDP or MA-PD plan.[179] Congress specified that the "plan specific enrollment weighted amount" is determined by reference to the Part D negotiated price.[180] As such, Congress made clear that the "plan specified enrollment weighted amount" is to be determined by reference to CMS's policies governing the Part D negotiated price.

This is not what CMS proposes. In the Part D context, CMS has long defined the Part D negotiated price to be "inclusive of all price concessions from network pharmacies, except those contingent price concessions that cannot reasonably be determined at the point-of-sale"—but not to require inclusion of price concessions from manufacturers.[181] Rather, PDPs and MA-PDs may choose to include manufacturer price concessions in the Part D negotiated price to the extent that they are passed through at the point of sale: "Part D sponsors are allowed, but generally not required, to apply rebates

[177] Initial Guidance at 17 (emphasis added).
[178] *See* Initial Guidance at 45.
[179] SSA § 1194(c)(1) (A), (B)(i).
[180] *Id.* § 1194(c)(2).
[181] 42 C.F.R. § 423.100 (emphasis added). CMS has issued a rule that will revise the Part D negotiated price definition effective January 1, 2024. But such revision does not alter the fact that the Part D negotiated price does not require inclusion of manufacturer price. *See* 87 Fed. Reg. 27,704, 27,899 (May 9, 2022).

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and other price concessions at the point of sale to lower the price upon which beneficiary cost-sharing is calculated."[182]

CMS's Initial Guidance ignores this long-standing policy defining the Part D negotiated price. For purposes of calculating the MFP ceiling under the option specific Part D drugs, CMS instead proposes to use Direct and Indirect Remuneration (DIR) data—rather than solely PDE data—to calculate the "plan specific enrollment weighted amount."[183] Notably, unlike PDE data, DIR data reflect all price concessions, including those received from manufacturers that are not passed through at the point of sale.[184]

CMS's proposed approach is contrary to statute, which makes clear that the MFP ceiling option must be determined by reference to the Part D negotiated price. By choosing expressly to define the MFP ceiling option by reference to the Part D negotiated price, Congress required such option to be calculated in accordance with policy governing the calculation of the Part D negotiated price. Any contrary approach would render meaningless Congress's express choice to use the Part D negotiated price as the statutory reference point.

In addition to being inconsistent with statutory text and Congressional intent, CMS's proposal also would create significant unnecessary complexities. It would be more burdensome for the Agency to determine the MFP ceiling for Part D drugs if the Agency were to apply a standard that is inconsistent with the Part D standard. In addition, it would impose a new and unfamiliar approach on pharmacies, plans, pharmacy benefit managers (PBMs), manufacturers, and other stakeholders, and would thereby increase the risk of confusion or error that could result in an erroneous MFP.

BIO urges CMS to abandon this proposal and instead align the Part D drug-specific MFP ceiling option with CMS's long-standing policy defining the Part D negotiated price, consistent with the requirements of the statute.

VI. Providing Access to the MFP

A. Background

Under the Negotiation Program, the manufacturer of a selected drug must provide access to the MFP to:

[182] 87 Fed. Reg. at 27,835 (the Part D negotiated price is "the price paid to the network pharmacy or other network dispensing provider for a covered Part D drug dispensed to a plan enrollee that is reported to CMS at the point of sale by the Part D sponsor").
[183] Initial Guidance at 40.
[184] CMS, Medicare Part D – Direct and Indirect Remuneration (DIR) (Jan. 19, 2017).

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- With respect to a Part B drug, "hospitals, physicians, and other providers of services and suppliers with respect to [individuals who are enrolled under Part B, including individuals who are enrolled in an Medicare Advantage (MA) plan, if payment may be made under Part B for the drug, and who are furnished the drug];"[185] and
- With respect to a Part D drug, "[individuals who are enrolled in a PDP or MA–PD plan if the drug is covered under such plan, and who are dispensed the drug,] at the pharmacy, mail order service, or other dispenser at the point-of-sale of such drug (and . . . to the pharmacy, mail order service, or other dispenser, with respect to such . . . individuals who are dispensed such drugs)."[186]

MFP-340B duplicate discounts are prohibited: The manufacturer is required to provide access to either the MFP or the 340B price, whichever is lower.[187]

B. MFP rebate model

BIO commends CMS for proposing that access to the MFP may be provided through an MFP rebate model and urges the Agency to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that a manufacturer may provide access to the MFP by either (1) ensuring that the price paid when acquiring the drug is no greater than the MFP or (2) providing retrospective reimbursement for the difference between the acquisition cost and the MFP.[188] BIO commends this approach.

Generally speaking, the manufacturer of a selected drug must provide access to the MFP to providers and pharmacies with respect to Part B, MA, and Part D beneficiaries.[189] It follows that the manufacturer has no obligation to provide access to the MFP to providers and pharmacies on units that will be furnished or dispensed to individuals who are not Part B, MA, or Part D beneficiaries (MFP-ineligible individuals).

An MFP rebate model is vital because it enables prospective safeguarding against diversion of MFP units to MFP-ineligible individuals. This is essential because the statute does not provide any retrospective

[185] SSA § 1193(a)(3)(B); *see also id.* § 1191(c)(2)(B).
[186] *Id.* § 1193(a)(3)(A); *see also id.* § 1191(c)(2)(A).
[187] *Id.* § 1193(d).
[188] Initial Guidance at 40.
[189] *Id.* § 1193(a)(3); *see also id.* § 1191(c)(2).

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mechanism for doing so. For example, the statute does not provide any post-hoc audit right to either the manufacturer or CMS to validate that providers and pharmacies have appropriately furnished or dispensed MFP units. Nor is there any post-hoc dispute resolution mechanism that enables the manufacturer to contest and recover the MFP discount on units that were improperly furnished or dispensed. Likewise, the statute does not grant CMS authority to impose CMPs or other sanctions, such as termination of access to the MFP, on providers and pharmacies that engage in diversion. Under these circumstances, CMS must establish a means to prospectively prevent diversion of MFP units. Authorizing an MFP rebate model is the most logical and practical means of doing so. It provides a mechanism through which the manufacturer can confirm that a unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP.[190]

Absent an MFP rebate model, there would be no way to mitigate against unlimited diversion of MFP units. And this is not a merely theoretical concern. In contrast to the Negotiation Program, the 340B Program, which is generally administered via upfront discounts, features a statutory audit right, a statutory dispute resolution mechanism, and agency authority to impose sanctions, including termination of access to the 340B price.[191] Yet even this constellation of statutory safeguards against diversion has proven deeply inadequate to prevent diversion of 340B units.[192] In the face of this well-documented real world experience, it would be patently unreasonable if CMS were to require upfront MFP discounts with no such safeguards. Indeed, doing so would be impermissible, as it would be tantamount to nullifying the express limitation on the obligation to provide access to the MFP only with respect to MFP-eligible individuals.[193]

A rebate model is also the most administratively straightforward means of providing access to the MFP. The rebate model is commonplace in the commercial sector and under Part D, such that an MFP rebate model can be implemented as seamlessly and efficiently as possible and in a manner well familiar to all

[190] As a manufacturer can confirm when it submits its "process for making the MFP available," Initial Guidance at 32, the minimum necessary Medicare claims data will be used to validate eligibility for the MFP, and reasonable time frames for submission of a request for, validation of eligibility for, and payment of an MFP rebate will be established. Additionally, providers and pharmacies will know at the time that a unit of a drug is furnished or dispensed that the drug is a selected drug and its associated MFP-based cost-sharing. As such, an MFP rebate model will not interfere with timely access by MFP-eligible individuals to MFP-based cost-sharing.

[191] PHSA § 340B(a)(5)(C), (d)(2)(B)(v), (3).

[192] *See, e.g.*, Examining HRSA's Oversight of the 340B Drug Pricing Program: Hearings Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce, 115th Cong. 2–3 (2017) (noting limited oversight against diversion and that between 63 and 82 percent of audited 340B covered entities have been found to be noncompliant with at least one program requirement) (statement of Rep. Tim Murphy), *available at* https://www.congress.gov/115/chrg/CHRG-115hhrg26929/CHRG-115hhrg26929.pdf; T. Okon, *Hospitals and for-profit PBMs are diverting billions in 340B savings from patients in need*, Stat News, https://www.statnews.com/2022/07/07/for-profit-pbms-diverting-billions-340b-savings/ (June 7, 2022); *see also* PHSA § 340B(a)(5)(B).

[193] *Whitman v. Am. Trucking Ass'ns, Inc.*, 531 U.S. 457, 484 (2001) (an agency may not implement a statute in a manner that "completely nullifies" an otherwise applicable provision).

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stakeholders. And CMS has clear legal authority to permit an MFP rebate model, as the statute does not specify how the manufacturer of a selected drug must provide access to the MFP, and, what is more, the statute grants CMS broad discretion to "establish[] . . . procedures to carry out the provisions of [the Negotiation Program], as applicable, with respect to [MFP-eligible individuals]."[194]

To ensure smooth integration of the rebate model, and because only pharmacies know the actual acquisition cost (AAC), BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

BIO is concerned with the metric CMS is proposing to use when defining the MFP discount, the AAC. CMS proposes that manufacturers that provide access to the MFP using a rebate model will need to provide the pharmacy a discount equal to the difference between the pharmacy's acquisition cost, or the AAC, and the MFP. Among others, there are concerns with accessibility of the pharmacy's AAC as it is currently not known to entities beyond the pharmacy. BIO recommends CMS define the MFP discount using a publicly reported metric, such as wholesale acquisition cost (WAC).

To facilitate a functional rebate model, BIO urges CMS to clarify that the proposed fourteen-day period during which an MFP rebate must be paid runs from the date on which the manufacturer has validated eligibility for the rebate.

CMS proposes that the manufacturers provide retrospective reimbursement within fourteen days. But the Initial Guidance is silent on when the clock begins to run. CMS should clarify that the clock begins to run on the date on which the manufacturer has validated eligibility for the rebate, in accordance with commercial sector conventions. In fact, this is the only rational starting point.

If CMS were instead to suggest that the clock begins to run on the date on which the rebate is requested, there would be insufficient time for the manufacturer to confirm that the unit was in fact furnished or dispensed to an MFP-eligible individual before providing access to the MFP—and, more fundamentally, no incentive for a provider or pharmacy to provide any validating Medicare claims data (including the 340B and non-340B claims modifiers discussed in section VI.C). This would render the rebate model completely nugatory, as such data are essential to the rebate model. Alternatively, we believe CMS should require providers to furnish claims level data such that it is required to process an individual claim, including the 340B or non-340B claims modifier as necessary. As CMS notes in its communication to states entitled, "Best Practices for Avoiding 340B Duplicate Discounts in Medicaid," manufacturer access to claims level data is likely needed for invoice validation.[195]The rebate model is

[194] SSA § 1196(a)(3).
[195] Best Practices for Avoiding 340B Duplicate Discounts in Medicaid, CMS, January 8, 2020. https://www.hhs.gov/guidance/sites/default/files/hhs-guidance-documents/cib010820_1.pdf.

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useful only to the extent that it provides a meaningful opportunity to prospectively safeguard against statutorily prohibited diversion of MFP units to MFP-ineligible individuals. As such, the rebate payment clock must begin ticking only after the manufacturer has verified the propriety of the rebate. Any contrary approach would be both plainly irrational and run directly contrary to the clear intent of Congress, which declined to impose any obligation on the manufacturer to provide access to the MFP with respect to an MFP-ineligible individual.[196]

To promote efficiency and program integrity and to minimize the burden on interested parties, CMS should adopt a third-party administrator or clearinghouse rebate model.

Finally, BIO strongly urges CMS to utilize a CMS-established third-party administrator (TPA) for the rebate model. By utilizing a TPA, CMS can ensure prompt payment while promoting efficiency and program integrity and minimizing obligations on stakeholders. The CMS-established TPA would also need to serve as a Medicare claims data clearinghouse. To enable manufacturers that choose the rebate option to validate the propriety of MFP rebate invoices, CMS should require all necessary claims level data be shared with the clearinghouse such that it is required to process an individual claim, including the 340B or non-340B claims modifier. The TPA clearinghouse would also be an effective way to ensure non-duplication between the MFP and the 340B program.

C. MFP-340B Duplicate Discounts

To prevent MFP-340B duplicate discounts, BIO urges CMS to condition payment of a claim for reimbursement for a unit of a selected drug on the accurate use of *either* a 340B *or* a non-340B claims modifier, across Part B, MA, and Part D.

As set forth above, the statute prohibits MFP-340B duplicate discounts.[197] To make this statutory prohibition meaningful, CMS must establish a mechanism that meaningfully allows manufacturers to avoid MFP-340B duplicate discounts across Part B, MA, and Part D.

With respect to Part B, CMS has already taken steps toward establishing such a mechanism. Effective January 1, 2024, all 340B covered entities that submit a Part B claims must use a 340B claims

[196] In the alternative to requiring payment of an MFP rebate within fourteen days of the date on which the manufacturer has validated eligibility for the rebate, CMS could requirement payment of an MFP rebate either (1) within thirty days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data, to be tolled during the pendency of a reasonable dispute resolution process or (2) within 45 days of the date on which the provider or pharmacy submits all necessary validating Medicare claims data. Notably, if the clock were to begin to run before the submission of such data, it would render the rebate model pointless, as the entire point of the model is to enable the manufacturer to validate eligibility for the rebate.
[197] *Id.* § 1193(d) (the manufacturer is required only to offer the lower of the MFP and the 340B price).

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modifiers.[198] With respect to Part D, CMS has similarly proposed to require a 340B identifier in prescription drug event (PDE) file, acknowledging that "requiring that a 340B indicator be included on the [PDE] record is the most reliable way to identify drugs that are subject to a 340B discount that were dispensed under Medicare part D," for purposes of excluding 340B units from the Part D inflation rebate calculation.[199]

BIO appreciates these steps, but CMS must take additional steps to make the prohibition of MFP-340B duplicate discounts meaningful. As a start, CMS must require the use of either a 340B modifier or a non-340B modifier, and condition payment of a claim on the accurate use of the applicable modifier. And CMS must implement the same constellation of essential safeguards with respect to MA units. All such safeguards are necessary to ensure that 340B covered entities are properly incentivized to accurately identify 340B units. And such safeguards must be paired with an MFP rebate model to prospectively guard against MFP-340B duplicate discounts, given the absence of a statutory mechanism for retrospectively doing so.[200] Any other safeguards necessary to protect against MFP-340B duplicate discounts should be adopted as well.

The need for such protections is readily apparent in light of the long history of improper duplicate discounts in analogous contexts: There continues to be widespread 340B covered entity non-compliance issues with respect to the MDRP-340B duplicate discount prohibition.[201] The same risk is present with respect to MFP-340B duplicate discount, and CMS must establish a mechanism to guard against them, as the prohibition against MFP-340B duplicate discounts is meaningful only if CMS does so. "An administrative agency cannot abdicate its responsibility to implement statutory standards under the guise of determining that inaction is the best method of implementation."[202]

D. Providing access to the MFP to Part D beneficiaries at the point of sale

BIO concurs with CMS that a manufacturer is not required to provide access to the MFP to Part D beneficiaries at the point of sale *directly*.[203]

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[198] CMS, Part B Inflation Rebate Guidance: Use of the 340B Modifiers 1 (Dec. 20, 2022), *available at* https://www.cms.gov/files/document/part-b-inflation-rebate-guidance340b-modifierfinal.pdf.
[199] CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum 18 (Feb. 9, 2023), *available at* https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf.
[200] *See* § VI.B *supra*.
[201] *See, e.g.*, Government Accountability Office, *Drug Discount Program: Federal Oversight of Compliance at 340B Contract Pharmacies Needs Improvement* (2018), *available at* https://www.gao.gov/assets/gao-18-480.pdf; *see also* PHSA § 340B(a)(5)(A).
[202] *United States v. Markgraf*, 736 F.2d 1179, 1183 (7th Cir. 1984).
[203] Initial Guidance at 31.

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In the Initial Guidance, CMS correctly recognizes that access to the MFP must be provided to Part D beneficiaries at the point of sale through PDPs or MA-PDPs, as opposed to the manufacturer (as a literal reading of the statute might suggest).[204] This is because it is impossible for a manufacturers to provide access to the MFP to Part D beneficiaries at the point of sale directly because they are not a party to the transaction at the point of sale. Rather, the point-of-sale transaction is among the Part D beneficiary, the pharmacy, and the plan or its PBM. Not only are manufacturers not a party to the transaction at the point of sale, but they are also typically not even in privity of contract with the point-of-sale pharmacy (and may also not even be in privity of contract with the plan or its PBM). As such, the only rational way to operationalize the statutory directive is for CMS to establish a pathway by which the MFP is passed through to Part D beneficiaries by those that are parties to the point-of-sale transaction. Therefore, BIO concurs with CMS's clarification that access to the MFP by Part D beneficiaries at the point of sale will be effectuated through plans, not manufacturers.

E. Application of the MFP Across Dosage Forms and Strengths

We request that CMS simplify its proposed approach and address concerns with its proposed methodology.

In section 60, CMS proposes a complicated set of comparisons for purposes of creating a single proposed MFP for each drug for negotiation purposes. BIO understands the agency's application of the statutory directive to create a "maximum fair price across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." However, the agency's decision, discussed above to treat products that are the subject of discrete NDAs as the same drug because they have the same active moiety, unnecessarily compounds the complexity of this effort. In many cases, products requiring significantly different routes of administration treat different conditions or have different clinical profiles—which results in a requirement for discrete NDAs to establish that the use of these therapies is safe and effective. In addition, drugs with different routes of administration may have substantially different manufacturing costs.

Thus, while BIO understands what the agency was attempting to accomplish in the system it has proposed for resolving the calculation of MFP across all dosage forms and strengths, the complexity of the system is compounded by CMS' desire to include, in a single calculation, products with multiple routes of administration that will often be approved under multiple NDAs as separate drugs. The calculation also relies upon standardized concepts of 30-day equivalent supply, which may or may not have a true equivalence, especially for any products with some formulations dosed once via injection to

[204] SSA § 1193(a)(3).

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last a longer period of time which may not be standardized across all clinical practice—and may differ markedly from oral formulations for the same chemical. The complicated equation CMS has established may not be able to adequately resolve these differences when calculating a standardized MFP across all forms and strengths of particular chemical compounds—and it need not do so for products approved under separate NDAs that should be treated as different drugs for purposes of MFP calculations.

BIO urges CMS to simplify MFP calculations by following the statutory language of the IRA and attempt to create a single MFP only for dosage forms of each drug that are identified by reference to the same NDA or BLA. Products that are separately approved should be treated as separate drugs. This will resolve much of the unnecessary complexity in the agency's proposed calculations described in section 60.

In addition, BIO is concerned that the last step of the 10-step process CMS has outlined will create an additional round of price cuts on dosage forms and strengths which cost more than other dosage forms and strengths for the same product for purposes of these calculations. By selecting a single ceiling price for the MFP and then comparing it differentially to the NDC9 level ceiling prices for the different dosage form and strengths of products, CMS is effectively undermining its own "single" MFP ceiling. Products which cost more at the NDC9 level than the dosage form and strength level calculated in section 60.2.2 and 60.2.3 would be subjected to two rounds of cuts, one during the process outlined in section 60.5 and again during the negotiation process itself. This undermines the creation of a "single" MFP since the different dosage forms and strengths are not equally subjected to the two rounds of cuts. This could potentially penalize more expensive dosage forms and strengths and undermine the ability of manufacturers to continue to provide these products. Moreover, the differential impact of the CMS methodology across dosage forms and strengths could also result in inequitable patient cost sharing.

In sum, BIO urges CMS to consider ways to simplify its methodology for applying the MFP across different dosage forms and strengths to avoid these distortions. As noted, some of these issues could be mitigated if CMS treats products which are separately approved as separate drugs. In addition, BIO believes that the agency has the authority to apply the MFP using more simplified units of measure than the 30-day equivalent methodology CMS has proposed.

F. The Date on Which a Generic or Biosimilar Is Marketed and the Date on Which *CMS Determines* That a Generic or Biosimilar Has Been Marketed

It is imperative that CMS abandon its bona fide marketing standard. This standard for determining the date of marketing of a generic or biosimilar is incompatible with the statute and contrary to sound public policy. CMS should instead adopt a standard that consistently designates the MDRP "market

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date" as both the date on which a generic or biosimilar is marketed *and* the date on which *CMS determines* that a generic or biosimilar has been marketed.

The statute anchors multiple important provisions to either (1) the date on which a generic or biosimilar is marketed or (2) the date on which CMS determines that a generic or biosimilar is marketed.

With respect to the former date, a drug or biologic may be selected for negotiation only if, by the selected drug publication date, it is a qualifying single source drug—which excludes a drug or biologic with respect to which a generic or biosimilar is marketed.[205] In addition, a biologic subject to a delay in selection for negotiation is rendered ineligible for selection for negotiation if a biosimilar is marketed by the date that is two years what otherwise would have been the selected drug publication date.[206] And a biologic may not be subject to such a delay if more than one year has passed since the biosimilar was licensed and the biosimilar is not marketed.[207]

With respect to the latter date, most notably, a selected drug ceases to be subject to the MFP at the start of the year that is "at least 9 months after the date on which [CMS] determines that at least one generic or biosimilar has been marketed."[208] In addition, a drug or biologic ceases to be subject to negotiation if, by the end of the negotiation period, CMS determines that a generic or biosimilar has been marketed;[209] and a non-compliant manufacturer of a selected drug subject to an ongoing excise tax ceases to be subject to such tax on the date on which CMS determines that a generic or biosimilar has been marketed.[210]

In either case, the determination of the date of marketing of a generic or biosimilar is of enormous consequence throughout the program. CMS has stated its intent to use an ill-defined and complicated process to make what is in fact an entirely straightforward determination. CMS intends to review PDE data to determine whether a generic or biosimilar is marketed under a "bona fide marketing" standard that reflects CMS's subjective assessment of whether the degree of utilization of the generic or biosimilar represents "robust and meaningful competition."[211]

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[205] *Id.* § 1192(e)(1)(A)(iii); (B)(iii). The statute refers to a generic or biosimilar that is both approved or licensed and marketed. We focus only on the latter because the date of marketing should never fall before the date of approval or licensure.
[206] *Id.* § 1192(f).
[207] *Id.* § 1192(f)(2)(D)(iii).
[208] *Id*. § 1192(c)(1) (emphasis added).
[209] *Id*. § 1192(c)(2).
[210] Internal Revenue Code (IRC) § 5000D(b)(1)(B).
[211] Initial Guidance at 67. BIO notes that, in some cases, the Initial Guidance does not specify whether the Agency intends to use the bona fide marketing standard to determine the date of marketing. In particular, it is unclear whether CMS intends to use such standard with respect to provisions regarding delay in the selection of a biologic for negotiation. If CMS intends to use an alternative standard with respect to such provisions, it should clearly articulate such alternative and subject it to public comment.

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CMS's approach is deeply problematic for myriad reasons. Foremost is that the bona fide marketing standard is contrary to the plain language of the statute: CMS's standard is not rationally related to the actual date of marketing. As a definitional matter, marketing is "[t]he act[] . . . of bringing or sending a product or commodity to market."[212] As such, once the "action of buying or selling" has occurred, a product has necessarily been "marketed."[213]

CMS itself has long recognized that the date on which a product is "marketed" is an objective point-in-time determination of the date on which it is made available for sale in the commercial marketplace—including in the course of implementing other provisions of the IRA as well as under the Part D program which will source the data on which CMS intends to rely in effectuating its bona fide marketing standard. Mere months ago, CMS proposed to determine when a product is "marketed" for purposes of the IRA's Part D inflation rebates by reference to the "market date" that the manufacturer must report under MDRP.[214] In turn, under MDRP, CMS has long defined the "market date" of a product by reference to the date on which the product entered commercial distribution, consistent with the plain language definition of "marketed."[215] And, under the Part D program, which will source the PDE data on which CMS intends to rely in effectuating its bona fide marketing standard, CMS has recognized that the date on which a product is "release[d] onto the market" triggers certain coverage-related obligations[216]—which by necessary implication means that CMS will have already recognized that a product has been released onto market by the time such coverage-related obligations yield PDE data showing utilization of the product.

[212] Oxford English Dictionary, Definition of Marketing, https://www.oed.com/view/Entry/114186?rskey=36dfg4&result=2&isAdvanced=false#eid (last visited Mar. 19, 2023).
[213] *Id.*
[214] CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of SSA, and Solicitation of Comments, § 40.3 (Feb. 9, 2023), *available at* https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf; FDA, National Drug Code Directory (July 22, 2022), *available at* https://www.fda.gov/drugs/drug-approvals-and-databases/national-drug-code-directory#:~:text=Marketing%20start%20date%20is%20the,no%20longer%20in%20commercial%20distribution. With respect to the IRA's Part B inflation rebate, CMS proposed to determine when a product is "marketed" by reference to the "date of first sale" that the manufacturer must report for ASP purposes, which likewise is an objective point-in-time determination. CMS, 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, § 50.3 (Feb. 9, 2023), *available at* https://www.cms.gov/files/document/medicare-part-b-inflation-rebate-program-initial-guidance.pdf.
[215] 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); *see also* 42 CFR 447.502.
[216] CMS requires that Part D plan sponsor P&T committees "make a reasonable effort to review a new FDA approved drug product (or new FDA approved indication) within 90 days of its release onto the market and . . . make a decision on each new FDA approved drug product (or new FDA approved indication) within 180 days of its release onto the market, or a clinical justification will be provided if this timeframe is not met." Prescription Drug Benefit Manual, ch. 6 § 30.1.5 (emphasis added).

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CMS should not supplant wholesale the statute's objective point-in-time "marketed" standard with an extra-statutory standard based on the Agency's subjective judgment of sufficiency of utilization.[217] Such judgment is immaterial to whether a product is in fact marketed—i.e., is available to be bought and sold in the commercial marketplace.

Notably, Congress well knows how to statutorily impose a "bona fide" standard in the drug pricing context. Congress expressly established such a standard when amending the MDRP statute in 2010 to specify that only "bona fide" service fees are exempt from the calculation of AMP.[218] By contrast, Congress chose not to establish such a bona fide standard here. "[W]here Congress knows how to say something but chooses not to, its silence is controlling."[219]

CMS's extra-statutory bona fide marketing standard has vast legal implications. For example, as noted above, the date on which CMS determines that a generic or biosimilar has been marketed determines when the MFP terminates.[220] As such, through the bona fide marketing standard, CMS is effectively claiming for itself limitless discretion to prevent the MFP from timely (if ever) terminating, notwithstanding the fact that a generic or biosimilar has in fact come to market, based on the Agency's subjective assessment of whether PDE data show that the generic or biosimilar is utilized sufficiently. In addition, CMS is implicitly claiming for itself authority to re-institute an MFP after an MFP has been terminated, if the Agency concludes based on PDE data that utilization of the generic or biosimilar ceases to be "robust and meaningful."[221]

Such policies are completely untethered to anything in the text or structure of the statute and run directly contrary to Congress's intent to allow market-based competition to govern where a generic or biosimilar has come to market to compete with a drug or biologic.[222] The Agency's approach is therefore patently unlawful. "[N]either federal agencies nor the courts can substitute their policy judgments for those of Congress."[223] CMS's effort to do so here is "effectively the introduction of a whole new regime of regulation," which "is not the one that Congress established."[224]

The Agency's unlawful standard also necessarily yields an inaccurate determination of when a generic or biosimilar was marketed. The Agency's reliance on PDE data guarantees that there will be a time lag

[217] It is unclear, for example, whether CMS expects a generic or biosimilar to capture and maintain a certain percentage of the market.
[218] SSA § 1927(k)(1)(B)(i)(II) (as amended by Pub. L. No. 111–148, § 2503(a) (2010)).
[219] *Animal Legal Def. Fund v. U.S. Dep't of Agric.*, 789 F. 3d 1206, 1217 (11th Cir. 2015).
[220] SSA § § 1192(c)(2).
[221] *See* Initial Guidance at 67.
[222] *See, e.g.,* SSA § 1192(c)(1).
[223] *Brown & Williamson Tobacco Corp. v. FDA*, 153 F.3d 155, 176 (4th Cir. 1998), *aff'd*, 529 U.S. 120 (2000).
[224] *MCI Telecomms. Corp. v. Am. Tel. & Tel. Co.*, 512 U.S. 218, 114 (1994).

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between the actual date of marketing and the date of CMS's determination because it takes time for sales to be reflected in PDE data. Indeed, CMS's long-standing policy requiring Part D plan sponsors to determine whether to add a newly approved drug to their formulary within 180 days of its release onto the market ensures that the PDE data will not accurately reflect when the drug came to market. Many Part D plan sponsors will not add a newly approved drug to their formulary until the 180-day mark, and, thus, the first six months of PDE data following the market entry of the drug will necessarily reflect only very limited uptake.[225] And some plan sponsors may choose not add the drug to their formulary at all. In addition, even where plan sponsors add the drug to their formulary, widespread uptake of a new product does not occur overnight. After a new product is made available for sale, providers and patients typically transition to such product gradually as they become increasingly familiar with its benefits relative to pre-existing alternatives.[226] Such a product is in fact marketed during this uptake period, but CMS's standard ignores this fact and focuses instead on whether the product is adequately utilized, in contravention of the statutorily mandated standard.[227] Such shifts in utilization patterns over time do not mean that the market is not working as intended.

The Agency compounds these concerns with its intent to review PDE data only once per month for purposes of determining when the MFP terminates.[228] The Agency's approach virtually always ensures that there will be a lag between the actual date of marketing and the date of CMS's determination. This poses a significant concern with respect to when the MFP terminates. If there is a lag of even a single day between the actual date of marketing and the date of CMS's determination, a selected drug can be subject to the MFP for a full additional year. For instance, if, on April 1, a generic or biosimilar is in fact marketed on April 1, but CMS's determination of this fact is deferred until April 2, the selected drug is subject to the MFP for a full year longer than if CMS's determination had not been deferred.

It is imperative that CMS abandon its unlawful and ill-advised standard and instead adopt as its standard the "market date" reported under MDRP. The MDRP "market date" standard should be used for identifying *both* the date on which a generic or biosimilar is marketed *and* the date on which CMS determines that a generic or biosimilar has been marketed.

Under MDRP guidance, "market date" is "the earliest date the drug was first marketed under the application number by any labeler."[229] Manufacturers report this date when reporting MDRP pricing

[225] While plan enrollees may access a non-formulary drug via an exceptions process, access may not be immediate under such process; moreover, exception processes typically yield only a very small volume of utilization.
[226] *See* A. Lubby, Factors affecting the uptake of new medicines: a systematic literature review, 14 BMC Health Services Research 469 (2014) (describing the various factors that affect early uptake of new medicines).
[227] Other examples of deficiencies in CMS's approach include circumstances where low utilization is driven by uncontrollable factors such as supply shortages.
[228] Initial Guidance at 62.
[229] CMS, MDRP Data Guide § 5.15 (Apr. 2022).

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data. As such, the MDRP "market date" is a familiar construct to both CMS and manufacturers, and carries the additional benefit of ensuring consistency across MDRP and the Negotiation Program. And, unlike the "date of first sale" used for ASP reporting purposes, the MDRP "market date" is available for generics and biosimilars without regard to whether they are subject to ASP reporting.[230]

It is particularly critical that the Agency equate the date on which CMS determines that a generic or biosimilar has been marketed with the MDRP "market date" because, as noted above, the difference of a single day in the date of CMS's determination can result in the MFP being extended for a full additional year. Failing to do so would have a dramatic chilling effect on the development of generics and biosimilars. Manufacturers would be seriously disincentivized against investing in the development of such products if there is a risk that they would be forced to compete with the MFP for an unduly extended period of time. This, in turn, would defeat Congress's objective of encouraging the development of generic and biosimilar market competitors.

For all of these reasons, we strongly oppose CMS's extra-statutory bona fide marketing standard, and strongly urge CMS instead to adopt the MDRP "market date" as a uniform standard for identifying both the date on which a generic or biosimilar is marketed and the date on which CMS determines that a generic or biosimilar has been marketed.

VII. Other Issues

A. Selected Drugs and Inflation Rebates

BIO urges CMS to clarify that selected drugs are not subject to an inflation rebate.

In its Initial Guidance, CMS solicits comment on the application of Part B and Part D inflation rebates to selected drugs.[231] Notably, CMS asserts: "The Part B and Part D inflation rebate programs apply to selected drugs, regardless of the status of the drug as a selected drug. Alternatively said, whether a drug is a selected drug will have no bearing as to whether the drug is also subject to the Part B and Part D inflation rebate programs."[232] This assertion is incorrect. BIO asks CMS to clarify a selected drug is not subject to an inflation rebate.

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[230] The "date of first sale" is reported only for products subject to ASP reporting, and thus may not be available for all generics and biosimilars whose marketing is implicated by the Negotiation Program. By contrast, the "market date" reported under MDRP is more broadly reported and is thus the superior metric to use. *See* CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, Implementation of Section 1860D-14B of Social Security Act, and Solicitation of Comments, (Feb. 9, 2023), https://www.cms.gov/files/document/medicare-part-d-inflation-rebate-program-initial-guidance.pdf.

[231] Initial Guidance at 71.

[232] *Id.*

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By statute, the Part B inflation rebate calculation is based in relevant part on the amount by which "106 percent of the amount determined under paragraph (4) of [section 1847A(b) of the SSA] for [a part B rebatable drug] during the calendar quarter . . . . exceeds . . . the inflation-adjusted payment amount . . . for such part B rebatable drug during the calendar quarter."[233]

Importantly, the circumstances under which an amount is "determined" under paragraph (4) is dictated by section 1847A(b)(1) (paragraph (1)).[234] Specifically, paragraph (1) dictates a payment amount of, "in the case of a single source drug or biological . . . , 106 percent of the amount determined under paragraph (4) *or* in the case of such a drug or biological product that is a selected drug . . . , with respect to a price applicability period . . . , 106 percent of the maximum fair price . . . applicable for such drug and a year during such period."[235]

In other words, the payment amount for a selected drug is determined under paragraph (1), and such payment amount is determined without regard to paragraph (4). Rather, it is only the payment amount for a non-selected drug that is determined under paragraph (4).

It necessarily follows that the Part B inflation rebate calculation has no application to a selected drug. With respect to such a drug, there is no amount "determined under paragraph (4)," and therefore Part B inflation rebates have no applicability.

This is not surprising. There is no policy reason for Congress to apply inflation rebates to selected drugs. A manufacturer should not be obligated to pay an inflation rebate on a selected drug because Medicare expenditures on a selected drug are already constrained by the maximum fair price.[236] Thus, with respect to a selected drug, Medicare is shielded from the increase in expenditures occasioned by a price increase that outpaces inflation that an inflation rebate is intended to address. Medicare does not need to be made whole on account of such a price increase, and, thus, no inflation rebate should be due.

For all of these reasons, CMS should clarify that a selected drug is not subject to an inflation rebate.

[233] SSA § 1847A(i)(3) (emphasis added).
[234] *See id*. § 1847A(b)(1).
[235] *Id*. § 1847A(b)(1)(B) (emphasis added).
[236] *Id*. §§ 1847A(b)(1)(B); 1860D-2(d)(1)(D).

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B. MFP and ASP

BIO urges CMS to amend its regulatory definition of "unit" to exclude MFP units from the ASP calculation.

By statute, MFP units are included in Best Price.[237] Sales included in Best Price are also generally included in ASP.[238] Thus, in the ordinary course, MFP units would be included in the ASP calculation. But the inclusion of MFP units in the ASP calculation would have vast and dire consequences for patient access.

The inclusion of MFP units in the ASP calculation would increasingly deflate ASP over time. As a result, ASP-based provider reimbursement would increasingly become inadequate to cover providers' acquisition costs. Eventually, providers would be left financially underwater if they were to furnish a selected drug to an MFP-ineligible individual, creating a very real risk that providers would no longer furnish such drugs to such individuals. And this vital threat to patient access to necessary medicines would be far-reaching. ASP is a reimbursement benchmark commonly used by non-Part B payers with respect to Part B drugs. As such, although Part B reimbursement for selected drugs will not be based on ASP, this would negatively affect countless individuals insured by non-Part B payers.

Fortunately, CMS has clear legal authority to prevent this. The ASP statute unambiguously confers on CMS broad authority to define "unit" for purposes of the ASP calculation "as . . . [CMS] determines appropriate."[239] CMS undoubtedly may exercise such authority to exclude MFP units from the ASP calculation to avoid the patient access concern described above.

The legislative history of the ASP statute makes abundantly clear that Congress intended for CMS to exercise such discretion in this way in precisely this sort of circumstance. When Congress delegated CMS the authority to define "unit" for purposes of the ASP calculation, it specifically stated that it was doing so to allow for the exclusion of "those sales that do not reflect market prices" from ASP.[240] By definition, MFP units do not reflect market prices.

There is also clear Agency precedent for excluding units that do not reflect market prices from the ASP calculation. In 2005, CMS carved Competitive Acquisition Program (CAP) units out of the ASP exclusion by excluding such units from the "unit" definition.[241] In doing so, CMS noted that ASP and CAP prices

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[237] *Id.* § 1927(c)(1)(C)(ii)(V).
[238] *See id.* § 1847A(c)(2)(A); *see also* 42 C.F.R. § 414.804(a)(1), (4)(i).
[239] SSA § 1847A(b)(2)(B).
[240] *See* H.R. Rep. No. 108-391, at 587–88 (2003).
[241] 70 Fed. Reg. 39,021, 39,077 (Jul. 6, 2005); *see also* 74 Fed. Reg. 61,738, 61,915 (Nov. 25, 2009).

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were "intended to be alternatives to each other" and, thus, CAP units should not be included in the ASP calculation.[242]

Identical reasoning supports excluding MFP units from the ASP calculation. MFP units do not reflect market prices: Rather, the MFP is a government-set price. Further, the MFP functions as an alternative to ASP: Part B will reimburse providers based on the MFP in lieu of ASP.[243]

For all these reasons, sound policy dictates that CMS exclude MFP units of selected drugs from the ASP calculation. BIO urges CMS to do so well in advance of the first IPAY to avoid any confusion and potential destabilization on non-Medicare markets once MFPs go into effect for the first set of selected drugs.

C. Civil Monetary Penalties (CMPs)

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed given the ambitious timelines in the statute and to allow manufacturers a reasonable time period to cure deficiencies before CMPs are imposed. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.

Under the IRA, CMS can impose CMPs on drug manufacturers for the following infractions related to the Part D Drug Negotiation program:

- **Refusing Access to MFP Price:** CMS will impose a CMP of 10 times the amount equal to number of units of drug furnished multiplied by the difference between the price for such drug made available to MFP-eligible entities on a Primary Manufacturer of a selected drug that has entered into an Agreement with CMS and fails to provide access to a price that is less than or equal to the MFP to MFP-eligible individuals dispensed the selected drug to pharmacies, mail order services, or other dispensers with respect to MFP-eligible individuals who are dispensed the selected drug or to hospitals, physicians, or other providers or suppliers that furnish or administer the selected drug to MFP-eligible individuals.

- **Failure to Comply to Requirements**: Any Primary Manufacturer of a selected drug that has entered into an Agreement with that fails to comply with requirements determined by CMS to be necessary for the purposes of administering the Negotiation Program and monitoring

[242] 78 Fed. Reg. at 61,915.
[243] SSA § 1847A(b)(1)(B).

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compliance with the Negotiation Program will be subject to a CMP of $1,000,000 for *each day* of such violation.

- **Provision of False Information:** If CMS determines that any manufacturer knowingly provides false information under the procedures to apply the aggregation rule for the Small Biotech Exception, such manufacturer shall be subject to a CMP equal to $100,000,000 for each item of such false information. Likewise, if CMS determines that any Biosimilar Manufacturer knowingly provides false information under the procedures to apply the aggregation of the Biosimilar Delay, the manufacturer shall be subject to a CMP equal to $100,000,000 for each item of such false information.

CMS will provide notice to the manufacturer with information regarding the CMP in accordance with section 1128A of the Act, including the option to either pay the CMP or to request a hearing as outlined in section 1128A. The CMP notice will include: Basis for the CMP; CMP amount due; Deadline for the manufacturer to respond with a hearing request or submit the CMP payment; Method to submit CMP payment(s); and Information on the right to request a hearing

The manufacturer will have 60 days from the date of receipt of the CMP notice to request a hearing—If the manufacturer does not request a hearing within 60 days, the CMP will be considered due on day 60 following the date of receipt of the CMP notice.

BIO urges CMS to proceed with caution on the implementation of CMPs as proposed. By any recognition, the time frames in statute for implementation of myriad sweeping changes in multiple parts of the Medicare program are ambitious. To make analogies to another program, BIO reminds CMS that a final rule to impose CMPs on drug manufacturers as part of the 340B program in 2017 was delayed multiple times. Although the 2017 Final Rule was scheduled to take effect on March 6, 2017, HRSA delayed the implementation of the rule multiple times. The Agency ultimately postponed the effective date of the rulemaking until July 1, 2019, to allow for "necessary time to consider more fully the substantial questions of fact, law, and policy identified by the Department during its review of the rule."

We similarly urge CMS to proceed cautiously with the imposition of CMPs on drug manufacturers and urge all stakeholders to work in good faith to comply with the statutory requirements of data reporting. To this end, we request that CMS send a notice of intent to impose a CMP and a reasonable period to cure the deficiency and/or to dispute the basis for the CMP, before any imposition of a CMP. The IRA imposes a tremendous amount of data reporting on drug manufacturers and puts them at risk for significant financial penalties. It will take time for manufacturers, especially small manufacturers, to comply in good faith with all the necessary data collection requests in the first years of the Negotiation program. And in no case should the Agency impose a CMP prior to finalization of relevant regulations.

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D. Negotiation Program Agreement

BIO urges CMS to ensure that the text of the Negotiation Program Agreement is made available for public comment at least sixty days in advance of the first selected drug publication date. Further, CMS should abandon its "Primary Manufacturer" and "Secondary Manufacturer" construct as part of the Agreement as it is impracticable and has no legal basis.

The Initial Guidance states that the Agency will make "reasonable efforts" to make the final text of agreement available to the public before the first selected drug publication date.[244] It is imperative that CMS make the text of the agreement available for public comment and do so well in advance of when manufacturers will be required to execute the agreement.

Advance notice of, and an opportunity comment on, the precise content of the Negotiation Program Agreement is vital because manufacturers are subject to CMPs of $1 million dollars per day for a violation of a terms of the agreement.[245] What is more, manufacturers that decline to enter into the Negotiation Program Agreement are subject to punitive excise taxes, such that manufacturers are effectively compelled to enter into the agreement.[246] Under these circumstances, it is imperative that CMS provide advance notice of, and an opportunity to comment on, the exact terms of the Negotiation Program Agreement. Manufacturers must be reasonably apprised of the specific obligations to which CMS proposes they be subject, and have reasonable opportunity to comment thereon, when compliance is enforced via such extraordinary sanction.

Advance notice is necessary at a minimum because manufacturers may need lead time to establish new processes in order to be prepared to comply with the terms of the agreement. CMS cannot put manufacturers in the untenable position of being subject to sanction for failing to comply with requirements that they cannot fulfill because the Agency did not supply adequate advance notice. Courts have long recognized that "[i]mpossible requirements imposed by an agency are perforce unreasonable" and therefore arbitrary and capricious.[247]

We also reinforce our earlier comments regarding CMS's proposal to hold a "Primary Manufacturer" responsible for submitting applicable information concerning a "Secondary Manufacturer." CMS also proposes, among other things, to require that "Primary Manufacturers" ensure that "Secondary Manufacturers" make the MFP available to MFP-eligible entities individuals and other entities, and CMS would impose CMPs on "Primary Manufacturers" for noncompliance by "Secondary Manufacturers." We

[244] Initial Guidance at 27.
[245] SSA § 1197(c).
[246] IRC § 5000D(b)(1)(A).
[247] *All. for Cannabis Therapeutics v. DEA*, 930 F.2d 936, 940 (D.C. Cir. 1991).

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urge CMS to abandon its proposed requirements under this "Primary Manufacturer" and "Secondary Manufacturer" construct. A Primary Manufacturer has no inherent legal authority to compel a Secondary Manufacturer to act or not act.

E. Patient Access and Part D Plan Formulary Placement

CMS should take steps to protect patient access to needed therapies in all Medicare Part D Plans.

By statute, Part D plans must place selected drugs on their formularies.[248] BIO recommends that CMS clarify how it will ensure robust beneficiary access to needed therapies, including selected drugs, and asks CMS to ensure safeguards that allow for diversity across formularies to meet patient needs. CMS should try to minimize class effects from the MFP process that would result in narrower formularies and provide fewer choices to patients. In addition, CMS should monitor plan coverage and tiering design, clinical appropriateness of utilization management policies, cost-sharing levels, and patient out of pocket exposure. BIO encourages CMS to update its oversight of formulary requirements and to re-examine Part D coverage determinations and appeals as well as tiering exceptions.

BIO appreciates this opportunity to provide feedback to CMS on the Initial Guidance. We look forward to continuing to work with the Agency on these important issues. Should you have any questions, please do not hesitate to contact Crystal Kuntz at 202-962-9200 or Ckuntz@bio.org.

Sincerely,

/s/

John Murphy
Chief Policy Officer

/s/

Crystal Kuntz
Vice President, Healthcare Policy & Research

[248] *Id.* § 1860D-4(b)(3)(I).