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August 17, 2026

VIA ELECTRONIC FILING – *IRARebateandNegotiation@cms.hhs.gov*

The Honorable Dr. Mehmet Oz
Administrator
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

Re: Medicare Drug Price Negotiation Program and Medicare Prescription Drug Benefit Program Proposed Rule (CMS-4215-P)

Dear Administrator Oz:

The Pharmaceutical Research and Manufacturers of America (PhRMA) appreciates the opportunity to respond to the Centers for Medicare & Medicaid Services' (CMS, the Agency) *Medicare Drug Price Negotiation Program and Medicare Prescription Drug Benefit Program Proposed Rule, CMS-4215-P* (the "Proposed Rule"),[1] which CMS released on June 16, 2026. PhRMA represents the country's leading innovative biopharmaceutical research companies, which are focused on developing innovative medicines that transform lives and create a healthier world. Together, we are fighting for solutions to ensure patients can access and afford medicines that prevent, treat and cure disease. PhRMA member companies have invested more than $900 billion in the search for new treatments and cures over the last decade, supporting nearly five million jobs in the United States.[2,3]

PhRMA has longstanding concerns about the impact of government price setting on patients, and our country's position as a leader in biopharmaceutical innovation. As it stands, the U.S. relies on a policy framework that balances incentives for innovation with robust competition following time-limited periods of intellectual property protection. Rather than permitting the government to dictate prices of medicines, the U.S. system has historically encouraged competition from other innovators, generic medicines and biosimilars—a framework that has consistently driven *down* prices over time. As a result of this framework, approximately 90 percent of prescriptions written in the U.S. are filled with generics and

[1] 91 Fed. Reg. 36236 (June 16, 2026).
[2] PhRMA. (August 2026). ICYMI: Biopharmaceutical Companies in American Hit New Investment Milestone. Available at: https://phrma.org/blog/icymi-biopharmaceutical-companies-in-america-hit-new-investment-milestone
[3] TEConomy. (May 2024) The Economic Impact of the U.S. Biopharmaceutical Industry: 2022 National and State Estimates. Available at: https://cdn.aglty.io/phrma/policy-issues/research-ecosystem/economy/The-Econ-Impact-of-US-Biopharma-Industry-2024-Report.pdf

biosimilars.[4] And because of this robust competition, prescriptions filled through Medicare and Medicaid cost 18 percent less, on average, than in other developed countries.[5]

Price setting of any kind—whether through the drug pricing provisions of the Inflation Reduction Act (IRA) or through other policies such as foreign reference pricing—would do irreparable harm to the U.S. biopharmaceutical ecosystem. The consequences of price setting are already evident in foreign countries, where governments rely on measures such as mandatory price cuts, revenue claw backs, and erosion of intellectual property protections to artificially suppress drug prices. When much of Europe adopted price controls nearly 40 years ago, the biopharmaceutical industry moved swiftly to the United States.[81] In 1986, European biopharmaceutical R&D investment exceeded that of the United States by 24 percent; today, decades after those controls took effect, Europe's R&D investment trails the United States by more than 40 percent.[83] In addition to the harm done to the European biopharmaceutical industry, today these countries have access to far fewer innovative medicines, and experience significant delays in accessing innovative medicines. Price setting of any kind will set the U.S. on a similarly dangerous path—and that path is no longer hypothetical. The IRA has already put the United States on it.

The IRA instructs CMS to implement the Medicare Drug Price Negotiation Program (MDPNP; the Program) through rulemaking starting with initial price applicability year (IPAY) 2029. This Administration has the opportunity through this rulemaking to mitigate the serious harms of the MDPNP, reduce the added harms of the practices first outlined by the Biden Administration in guidance and to provide a more durable, less damaging framework for the Program. Unfortunately, the proposed regulations not only do not move in a less damaging direction; they will exacerbate the damage that the MDPNP is already doing to innovation and patient access today.

Not only does the MDPNP undermine the competitive framework that enables U.S. leadership in global biopharmaceutical innovation, but also it has been a disaster for patient access and affordability, as well as innovation and competition. Price setting under the IRA has:

- **Harmed Biopharmaceutical Innovation:** Investments in R&D for small molecule medicines are expected to decrease by $232 billion over the next 20 years, resulting in an estimated 188 fewer small molecule medicine advances.[6] Indeed, empirical analyses have already observed a 25 percent drop in clinical trial activity for unapproved small molecule medicines since the IRA was enacted.
- **Undermined Competitive Market Dynamics.** By undermining incentives for generic entry, IRA price setting weakens the competition that typically lowers prices by 80 to 90 percent, potentially increasing the average price of many selected drugs over the long-term.[7]

[4] AAM. (September 2025). U.S. Generic and Biosimilar Savings Report. Available at: https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf
[5] Philipson T.J., Zhang D., Zhao Q. (June 2025). International Comparison of Prices for Drug Prescriptions. *The University of Chicago.* Available at: https://bpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2025/06/Policy-Brief-International-Price-Differences-for-Drug-Prescriptions-June-7.docx.pdf
[6] Philipson T.J., Ling Y., Chang R. (October 2023). The Impact of Price Setting at 9 Years on Small Molecule Innovation Under the Inflation Reduction Act. *The University of Chicago.* Available at: https://bpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2023/10/Small-Molecule-Paper-Final-Oct-5-2023.pdf
[7] Philipson T. et al. (August 2026). The Impact of Price Controls on Longterm Prescription Drug Prices. *The University of Chicago.* Available at: https://ecchc.economics.uchicago.edu/project/the-impact-of-price-controls-on-longterm-prescription-drug-prices/

- **Failed to Improve Affordability and Access:** Under the IRA, two-thirds of Medicare beneficiaries are enrolled in Part D plans where their cost sharing is expected to *increase* for many price-set drugs.[8]

We elaborate further on the MDPNP's harms and failures later in this letter.

Concerns with the Structure and Implementation of IRA Price Setting

In addition to the significant harm to current and future patients, the Proposed Rule creates additional bureaucracy within the Agency, promulgating legally binding rules that unnecessarily expand the burden of the MDPNP. Rather than streamlining and alleviating stakeholder burdens, the Proposed Rule adds to these burdens. Rather than providing relief to Americans who struggle to afford their medicines at the pharmacy counter, the Proposed Rule offers Americans insufficient protection from health insurance plans, which under IRA price setting have not changed the rate at which they deny access to new medicines in Medicare Part D.[9]

Further, the so-called "negotiation" as defined in the IRA and now proposed to be codified in regulations remains fundamentally misaligned and incompatible with a true negotiation process. Unfortunately, the framework set forth in both the IRA and the Proposed Rule diverge significantly from the principles and practices of genuine negotiation as seen in the private market—made worse by the fact that rulemaking beginning for IPAY 2029 aims to enshrine legally binding policies in the Code of Federal Regulations. The structure and implementation of the IRA's price setting provisions, including as articulated in the Proposed Rule, raise serious concerns about fairness, transparency, and legality:

- **The IRA's "negotiation" process as outlined in the Proposed Rule bears no resemblance to true negotiations.** Under the MDPNP, CMS wields unilateral authority to set medicine prices with minimal input from manufacturers, who face severe penalties—including market exclusion, exorbitant excise taxes, or civil monetary penalties—if they do not comply. Unlike true negotiations, where both parties engage in a mutual exchange and can walk away, CMS dictates terms through a rigid, non-negotiable framework that favors the Agency. Under the statute and the Proposed Rule, manufacturers are required to sign agreements before knowing the final price, cannot revise terms, and are denied legal recourse or transparency into CMS' decision-making process. This coercive structure lacks the flexibility, reciprocity and balance that define genuine negotiation—and now that this process would be administered through regulations that legally bind both the agency and manufacturers, the process is even further removed from any semblance of genuine, market-based negotiations.
- **CMS' methodology for setting prices lacks transparency and objective standards.** Rather than following a consistent, replicable process, CMS relies on a vague, opaque approach that provide no assurance that MFPs will reflect the therapeutic contributions of selected drugs. The Agency had an opportunity to provide innovators with meaningful certainty through this rulemaking process, yet it provides remarkably little clarity on how evidence is evaluated,

[8] Magnolia Market Access. When Lower Prices Don't Mean Lower Costs: How Part D Benefit Changes Are Shifting Out-of-Pocket Spending in 2026 Under the Inflation Reduction Act. Available at: https://www.magnoliamarketaccess.com/insight/medicare-part-d-cost-sharing-changes-2026/

[9] IQVIA. (August 2026). Rejection Rates Unchanged by MFP Drug Coverage Requirement. Available at: https://www.iqvia.com/locations/united-states/blogs/2026/07/rejection-rates-unchanged-by-mfp-drug-coverage-requirement

how factors are prioritized, or how final prices are determined. This opacity makes it nearly impossible for manufacturers, as well as patients and other stakeholders, to understand the outcome, and raises concerns about bias, inconsistency, and the potential for flawed or incomplete analysis. Without a transparent framework that binds the Agency, CMS can attempt to justify virtually any price below the statutory ceiling, undermining predictability and fairness.

- **The IRA unconstitutionally delegates legislative power to CMS.** As interpreted by CMS, the statute grants the Agency broad, unchecked authority to define key terms, impose penalties, and interpret statutory language without oversight. CMS has already expanded its reach by redefining what constitutes a "drug" and a "manufacturer" and "marketing" and by asserting control over entities not directly named in FDA applications. CMS fails to adhere to the plain meaning of text in reaching its expansive misinterpretations. This sweeping assertion of legislative power, combined with the continuation of the Biden Administration's expansive statutory interpretations, raises serious constitutional questions about separation of powers and the limits of executive authority, contradicting the Administration's commitment to ensuring all regulations are authorized by law.

* * *

The impact of the IRA's unilateral price setting is widespread, causing harm to patients, as well as innovation and market competition. In this letter, we articulate our core concerns with the MDPNP, as well as with CMS' implementation through the Proposed Rule, which have been further exacerbated by the Agency's continuation of policies first crafted by the Biden Administration that repeatedly overreach and fail to protect patients. Areas of concern addressed in more detail this letter and its Appendices include:

I. Harm to Biopharmaceutical Innovation
II. Undermining Competitive Market Dynamics
III. Failure to Improve Access and Affordability

In addition to outlining our core concerns with the Proposed Rule, we are attaching to this letter several Appendices that provide technical, in-depth input on specific issues. In many instances, the recommendations outlined in the Appendices are in addition to feedback that PhRMA has previously provided to CMS in other comment letters or forums. The topics they focus on are of great importance to PhRMA and its membership, and we welcome the opportunity to discuss them in more detail with CMS.

Appendix A: Identification of Selected Drugs (Subpart B);

Appendix B: Negotiation Program Agreement (Subpart C);

Appendix C: Program Administration (Subpart D);

Appendix D: Establishment of Single MFP and Determination of Ceiling (Subpart E);

Appendix E: Negotiation Process (Subpart F);

Appendix F: Renegotiation of an MFP (Subpart G);

Appendix G: Implementation of the MFP (Subpart H);

Appendix H: Manufacturer Compliance and Oversight, and Civil Monetary Penalties (Subparts J & K)

Appendix I: Proposed Implementation of Inflation Reduction Act Provisions for the Medicare Prescription Drug Benefit Program

PhRMA notes that CMS states in the preamble of the Proposed Rule that, "[u]nless otherwise specified, CMS proposes that the provisions herein would apply with respect to all initial price applicability years beginning with initial price applicability year 2029."[10] However, the regulation text does not contain such language. PhRMA recommends that CMS expressly provide an effective date in the regulatory text, for example, by inserting the preamble language into the general provisions of the proposed regulations at § 429.10.

I. Harm to Biopharmaceutical Innovation and Investment in Research & Development

The IRA and CMS' implementation of the Program fundamentally alter existing research and development (R&D) incentives and jeopardize the future development of medicines with very real consequences for patients and the broader health care system. Although impacts may vary by company, the IRA and CMS' interpretation of the statute are already discouraging innovation. Under the flawed IRA statute, small molecule medicines face price setting four years before biologic medicines. This so-called "pill penalty" discourages the development of treatments that are often the most accessible and critical for conditions like cancer, mental illness and chronic diseases. Since the IRA was introduced, early-stage investment in small molecules has plummeted by nearly 70 percent among smaller, early-stage biopharma companies.[11] Additionally, the number of clinical trials testing new small-molecule drug candidates have fallen 25 percent since the IRA passed.[12]

Because post-approval trials can take years to complete and require significant investment, biopharmaceutical companies are also shifting away from pursuing new indications for already FDA-approved treatments in disease areas where post-approval R&D has been indispensable. Since the IRA's enactment, monthly starts of industry-funded post-approval trials for small molecules have dropped 47.3 percent, a much steeper decline than for other medicine types.[13] For example, one study found more than 60 percent of small molecule cancer medicines approved between 2006 and 2012 received at least one post-approval indication, and nearly half of those occurred seven or more years after initial approval.[14] Similarly, another analysis examining cardiovascular medicines approved between 1995 and 2021 found 92 percent were small molecule medicines and among these, nearly half of approved indications were

[10] 91 Fed. Reg. 36237.
[11] Schulthess, D.G. et al. (April 2025). The Inflation Reduction Act's Impact Upon Early-Stage Venture Capital Investments. *Therapeutic Innovation & Regulatory Science* . Available at: https://doi.org/10.1007/s43441-025-00773-3.
[12] Long G. (March 2026) Trends in industry-sponsored clinical trial activity since passage of the Inflation Reduction Act. *Journal of Medical Economics.* Available at: https://www.tandfonline.com/doi/full/10.1080/13696998.2026.2646075
[13] Zheng H., Patterson J., Campbell J. (2025). The Inflation Act and Drug Development: Potential Early Signals of Impact on Post-approval Clinical Trials. *Therapeutic Innovation & Regulatory Science*, 1-9.
[14] PhRMA. (July 2023). Emerging Value in Oncology: How Ongoing Research Expands the Benefits of Oncology Medicines. Available at: https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/PhRMA_Emerging-Value-Report/PhRMA_Emerging-Value-Report_FIN-web_July2023_v2.pdf.

approved seven or more years after initial approval.[15] Unfortunately, many of these kinds of post-approval innovations may be forgone moving forward.

Definition of Qualifying Single Source Drug and Treatment of Fixed Dose Combination Products

CMS' interpretation of qualifying single source drug (QSSD) under the IRA is untethered from the statute and will stifle the development of innovative and lifesaving treatments by treating new dosage forms and formulations with the same active ingredient or moiety as the same medicine—even if they are approved under separate applications for different diseases or patient populations. Distinct new treatments could face immediate price setting upon approval, eroding the value of critical post-approval innovation and disincentivizing the development of new forms of medicines. One study showed that if CMS had applied this approach retroactively to novel medicines approved between 2006 and 2013, 110 unique medicines and biologics products could have been swept into price setting—more than double the intended 50 negotiation eligible drugs.[16] The consequences are already evident: for IPAY 2026, 2027 and 2028 CMS selected 16, 26 and 22 distinct new drug applications and biologics license applications, respectively, many with different brand names and some approved within two and a half years – far exceeding the statutory limits on the age of the selected drug.

CMS has now proposed to expand this flawed, unsupported interpretation of the statute to include not only products with the same active ingredient, but also fixed-dose combination products with a common active ingredient(s) if the differing active ingredient creates a new formulation that enables an alternative route of administration.[17] This policy directly undercuts incentives for innovation that can make medicines more patient-friendly and convenient, which can increase uptake, support adherence and ultimately lower other health care costs.

CMS should limit a QSSD to those drugs or biologics approved or licensed under the same NDA or BLA, either as part of the original application or under a supplement to such application. Further, the approval or licensure of any drug product or biological product must have occurred at least seven or 11 years, as applicable, to the selected drug publication date, meaning that the relevant supplement must be at least seven or 11 years old. CMS also should abandon its proposed special rule that singles out certain fixed combinations for disparate treatment without a statutory basis. Instead, CMS should take a uniform approach to all fixed-combination products such that a product containing only one, but not all, active moieties, active ingredient, or antigen components from the same NDA/BLA holder are not aggregated with formulations of the fixed combination and are considered separate QSSDs.

II. Harm to Competitive Market Dynamics

The U.S. market-based system is designed to balance innovation, access and cost containment by promoting robust competition among brand medicines, generics and biosimilars—driving down prices,

[15] Grabowski H., Long G. (March 2024). Post-Approval Indications and Clinical Trials for Cardiovascular Drugs: Some Implications of the US Inflation Reduction Act. *Journal of Medical Economics.* Available at: https://www.tandfonline.com/doi/full/10.1080/13696998.2024.2323903.

[16] Stratevi. (2025). Combining Apples and Oranges: An Examination of CMS' Methods for Defining a Qualifying Single Source Drug. Available at: https://static1.squarespace.com/static/621e5edfadb9950783f45d9a/t/67cf3ba77613db2190dfb3a6/1741634472366/Multiple+Forms+Policy+Brief.pdf.

[17] Proposed § 429.125(b)(4)(i).

and often reducing costs by 60 percent or more.[18] Competition among brand medicines alone has generated billions in savings, with one study showing that launches of new brand medicines between 2013 and 2017 led to over $10 billion in price reductions across 12 therapeutic classes.[19] Over time, this system delivers long-term savings as branded medicines are followed by generics and biosimilars, which now account for 90 percent of prescriptions and have saved $3.1 trillion over the past decade.[20]

Despite this success, the IRA and CMS' implementation of its price setting program threaten to dismantle these incentives by allowing the government to impose prices so low that generic and biosimilar manufacturers may no longer find it viable to enter the market. The IRA undermines the statutory framework that rewards first-to-market generics, weakening their ability to compete and recoup investments.

For biosimilars, the misalignment between MDPNP timelines and the 12-year exclusivity period under the Biologics Price Competition and Innovation Act, coupled with CMS' vague and extra-statutory "bona fide marketing" standard, creates profound uncertainty. With biosimilar development already requiring $100 million to $300 million in investment,[21] this lack of predictability may make future development financially infeasible, leading to fewer products on the market and potential medicine shortages while limiting competition.

Though the IRA includes a "Special Rule" to potentially delay selection and price setting of eligible biologics facing biosimilar competition, the IRA's language and CMS' interpretation of the law ultimately risk failing to provide biosimilar manufacturers with the assurances needed to invest resources for biosimilar development. Ultimately, by substituting price setting for competition, the MDPNP risks unraveling the very system that has delivered both innovation and affordability to patients. CMS also has unfortunately proposed in rulemaking to continue its ambiguous, extra-statutory "bona fide marketing" standard.[22] This concept, entirely invented by CMS, only serves to create significant ambiguity within the marketplace and is another example of CMS operating beyond the bounds of its statutory authority.

III. Failure to Improve Access and Affordability

As the implementation of the MDPNP has proceeded, we continue to see how the Program has eroded the success of the Medicare program and failed to solve the fundamental problems driving narrowing patient access and affordability challenges. Price setting undermines the ability of Medicare plan sponsors to negotiate with manufacturers, which is foundational to the competitive structure and success of Part D. At the same time, it does little to address health plan and pharmacy benefit manager abuses that harm patient access and increase out-of-pocket (OOP) costs.

[18] Hernandez, I. et al. (2024). Price benchmarks of drugs selected for Medicare price negotiation and their therapeutic alternatives. *Journal of Managed Care & Specialty Pharmacy.* Available at: https://doi.org/10.18553/jmcp.2024.24153.
[19] Dickson S., Gabriel N., Hernandez I. (August 2023). Changes in Net Prices and Spending for Pharmaceuticals After The Introduction Of New Therapeutic Competition, 2011–19. *Health Affairs*. Available at: https://www.healthaffairs.org/doi/10.1377/hlthaff.2023.00250.
[20] AAM. (2024). The U.S. Generic & Biosimilar Medicines Savings Report, 2024. Available at: https://accessiblemeds.org/resources/reports/2024-savings-report/.
[21] McKinsey. (August 2022). Three Imperatives for R&D in Biosimilars. Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars
[22] Proposed § 429.130.

In Medicare Part D, PhRMA and many other stakeholders have raised concerns over the past several years about increasingly restrictive trends in Medicare Part D formulary design and utilization management (UM), and the risks of how these trends would be exacerbated by MDPNP price setting.[23,24,25] This concern has since materialized – recent research shows that in the first quarter of 2026, patients attempting to initiate therapy with IPAY 2026 selected drugs for immunology and oncology faced initial rejection rates of 59 percent and 67 percent respectively.[26] This analysis also found that across the first ten selected drugs, denial rates remained largely unchanged after the law's price controls took effect.[27] Combined with significant reductions in plan choices and higher premiums, the program threatens affordable access to care for millions of beneficiaries. [28]

Moreover, while harming biopharmaceutical innovation, price-setting under the IRA is not translating into lower OOP costs for patients. In fact, analysis suggests that downstream effects of the program will cause patients to pay more for their medicines—for instance, under the IRA, two-thirds of Medicare beneficiaries are enrolled in Part D plans where their cost sharing is expected to increase for many price-set drugs because of shifts in plan coverage towards coinsurance and/or higher deductibles.[29] Further, actuaries project that nearly all (93 percent) of Part D beneficiaries are not expected to see OOP savings from the first ten price-set drugs.[30] The limited OOP impact of MFPs is expected to be even more pronounced in future IPAYs.[31] Despite a small fraction of Part D beneficiaries experiencing OOP savings from price setting, the vast majority (86 percent) of beneficiaries experienced an increase in either their premium, their deductible, or both in 2026 (78 percent of MA-PD enrollees and 97 percent of PDP enrollees).[32] While the implementation of the maximum out-of-pocket (MOOP) was transformative for affordability for the sickest and most vulnerable patients, the majority of Part D beneficiaries experience relatively low out-of-pocket costs: a recent analysis found that nearly 72 percent of non-low-income Part D beneficiaries who are not enrolled in employer plans had average out-of-pocket costs of less than $120 annually—or just ten dollars per month.[33] For beneficiaries managing multiple chronic and high-cost conditions, the Medicare Prescription Payment Plan (MPPP) remains a profoundly underutilized program, with only 3.8 percent of beneficiaries who reached the catastrophic phase and therefore would be likely to

[23] PhRMA. (March 2026). Insurers Routinely Block Seniors' Access to Medicines in Medicare Part D. Available at: https://phrma.org/blog/insurers-routinely-block-seniors-access-to-medicines-in-medicare-part-d.
[24] PhRMA. (January 2025). PhRMA Comments to CMS on Contract Year 2026 Medicare Advantage and Part D Proposed Rule. Available at: https://phrma.org/resources/phrma-comments-to-cms-on-contract-year-2026-medicare-advantage-and-part-d-proposed-rule.
[25] PhRMA. (April 2024). IRA Is Already Negatively Impacting Access to Medicines in Part D. Available at: https://phrma.org/blog/ira-is-already-negatively-impacting-access-to-medicines-in-part-d.
[26] IQVIA. (August 2026). Rejection Rates Unchanged by MFP Drug Coverage Requirement. Available at: https://www.iqvia.com/locations/united-states/blogs/2026/07/rejection-rates-unchanged-by-mfp-drug-coverage-requirement
[27] *Ibid.*
[28] Avalere Health. (October 2025). Part D Choices Continue to Shrink with Fewer PDPs in 2026. Available at: https://advisory.avalerehealth.com/insights/part-d-choices-continue-to-shrink-with-fewer-pdps-in-2026
[29] Magnolia Market Access (2026). When Lower Prices Don't Mean Lower Costs: How Part D Benefit Changes Are Shifting Out-of-Pocket Spending in 2026 Under the Inflation Reduction Act. Available at: https://www.magnoliamarketaccess.com/insight/medicare-part-d-cost-sharing-changes-2026/
[30] Milliman. (August 2026). Assessing the Beneficiary Out-of-Pocket Impact of the MDPNP. Available at: https://www.milliman.com/en/insight/assessing-beneficiary-out-of-pocket-impact-mdpnp
[31] *Ibid.*
[32] *Ibid.*
[33] Avalere. (July 2026). New Analysis Highlights Opportunities to Improve MPPP Uptake. Available at: https://advisory.avalerehealth.com/insights/new-analysis-highlights-opportunities-to-improve-mppp-uptake

benefit enrolling in 2025.[34] PhRMA provided recommendations to CMS in prior comments to improve MPPP uptake, and we encourage the Agency to focus efforts to address patient access and affordability concerns on MPPP improvement.[35,36]

Government price-setting and other provisions in the IRA are reshaping formulary dynamics, and plan responses threaten beneficiary access. The use of inappropriate UM by plans as a blunt instrument to contain costs in response to increases in plan liability will lead to further barriers to patient access by exacerbating already high provider burden, contributing to provider burnout, altering providers' clinical decision-making and driving patients to treatments that are not aligned with clinical guidelines or not suited for the individual patient when accounting for their unique characteristics.[37,38,39,40]

As described above, the IRA has already caused significant harm to patients and consumers through reduced access to medicines, higher premiums and OOP costs for price-set medicines, and reduced plan options. CMS should take new steps to solidify meaningful oversight of patient access in Part D, either through the IRA rulemaking process or the Part C/D rulemaking process, including recommendations provided by PhRMA in our comments on Program Guidance for IPAY 2028.

Under Medicare Part B, approximately nine in ten Medicare fee-for-service (FFS) beneficiaries are already enrolled in supplemental insurance plans that cover their out-of-pocket costs for Part B drugs. Because of that fact, combined with the number of Part B beneficiaries taking selected drugs, the program is expected to yield cost savings for less than one percent of Medicare FFS beneficiaries. Patient access to Part B selected drugs could also be under threat, as beginning in 2028, Part B medicines selected for negotiation under the IRA will have their market-based ASP replaced with a much lower MFP, resulting in lower reimbursement and add-on payments for selected drugs. This will be particularly harmful to community and independent providers, who may no longer be able to stock these medicines.

For more detailed legal and policy considerations on these issues, please see the attached technical appendices.

* * *

PhRMA appreciates your consideration of these comments. Please feel free to contact Elizabeth Carpenter (ecarpenter@phrma.org) and Jim Stansel (jstansel@phrma.org) if there is any further information we can provide or if you have any questions about our comments.

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[34] *Ibid.*
[35] PhRMA. (January 2025). PhRMA Comments to CMS on Contract Year 2026 Medicare Advantage and Part D Proposed Rule. Available at: https://phrma.org/resources/phrma-comments-to-cms-on-contract-year-2026-medicare-advantage-and-part-d-proposed-rule
[36] PhRMA. (September 2023). PhRMA Comments to CMS on Medicare Prescription Payment Plan Guidance. Available at: https://cdn.aglty.io/phrma/global/resources/import/pdfs/PhRMA%20Comments%20on%20MPPP%20Guidance_Final%2092023.pdf
[37] American Medical Association. (2024). 2024 AMA Prior Authorization Physician Survey. Available at: https://www.ama-assn.org/system/files/prior-authorization-survey.pdf.
[38] Salzbrenner S.G. et al. (July 2023). Influence of prior authorization requirements on provider clinical decision-making. *Am J Manag Care*. Available at: https://pubmed.ncbi.nlm.nih.gov/37523751/.
[39] Gracie J., Jimenez R., Winkfield K.M. (October 2024). The Burden of Insurance Prior Authorization on Cancer Care: A Review of Evidence From Radiation Oncology. *Adv Radiat Oncol*. Available at: https://pubmed.ncbi.nlm.nih.gov/39758976/.
[40] Struthers A. et al. (November 2024). Utilization management and physician burnout. *Am J Manag Care*. Available at: https://pubmed.ncbi.nlm.nih.gov/39546758/.

Sincerely,

/s/

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Elizabeth Carpenter

Executive Vice President, Policy and Research

/s/

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Jim Stansel

Executive Vice President and General Counsel

To the extent applicable to the present Proposed Rule, these technical appendices also incorporate PhRMA's prior comments on guidance for IPAY 2028, 2027 and 2026.

Appendix A: Identification of Selected Drugs (Subpart B)

The recommendations below reflect PhRMA's principal concerns with CMS' proposed interpretation of qualifying single source drugs (QSSDs), biosimilar competition provisions, generic and biosimilar market entry standards, orphan drug treatment and timing of generic or biosimilar entry.

Key Recommendations:

- Require that, for a drug or biological product to be included in a QSSD, it must be approved or licensed under the same NDA or BLA, either as part of the original application or under a supplement to such application. Further, the approval or licensure of any drug product or biological product must have occurred at least seven or 11 years (as applicable) prior to the selected drug publication date;
- Finalize 42 C.F.R. § 429.125(b)(4), but without the exception in proposed 42 C.F.R. § 429.125(b)(4)(i);
- Limit a QSSD to drug products/biological products that are approved/licensed under a single NDA/BLA;
- Ensure each drug product or biological product in a QSSD independently meets the age requirement;
- Apply a consistent approach for the purposes of identifying QSSDs and not adopt a special rule for certain fixed combinations involving a new route of administration;
- Provide a longer window of time for submitting initial delay requests and notice to the reference product manufacturer;
- Revise the “high likelihood” requirement, which is untethered from the statute, unworkably vague, and overly rigid;
- Undertake a predictable and flexible approach toward evaluating requests for the second one-year pause;
- Eliminate the “Bona Fide” qualifier;
- Align treatment of “Bona Fide Marketing” with other provisions of the IRA;
- Discontinue continual evaluation of “Bona Fide Marketing”;
- Apply the orphan drug exclusion based on a drug or biological product’s status at the time of the otherwise applicable selection date;
- Apply the orphan drug exclusion to the drug or biological products approved in a single NDA/BLA.

I. Identification of Qualifying Single Source Drugs (§ 429.125)

PhRMA opposes the overbroad interpretation of a qualifying single source drug (QSSD) that CMS used for initial price applicability year (IPAY) 2026, 2027 and 2028 and generally proposes to maintain under the Proposed Rule. PhRMA also opposes proposed 42 C.F.R. § 429.125(b)(4)(i), which would modify that interpretation through an exception for certain fixed-combination products at 42 C.F.R. § 429.125(b)(4)(i).

The statute defines a QSSD by reference to drug products and biological products approved or licensed under section 505(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) or section 351(a) of the Public Health Service Act (PHSA) and requires each such product independently to satisfy the applicable age requirement. Under *Loper Bright Enterprises v. Raimondo*, an agency is required to apply the "single, best meaning" of a statute, and the President has issued a memorandum on April 9, 2025, prioritizing the review and repeal pursuant to Executive Order 14219 of existing regulations that are unlawful under *Loper Bright.* CMS' current interpretation of the QSSD definition departs from the statutory text and fails to reflect the statute's single, best meaning by aggregating products based on active moieties or active ingredients and by measuring eligibility using the approval date of the earliest approved application, rather than the approval or licensure of the particular drug product or biological product at issue. By doing so, CMS sweeps together products approved under different new drug applications (NDAs) and biologic license applications (BLAs) and subjects products to selection before they have independently met the statutory seven- or eleven-year age requirement. As explained in subsection A below, CMS should revise its definition to align with the statute and *Loper Bright*. ***Specifically, CMS should require that, for a drug or biological product to be included in a QSSD, it must be approved or licensed under the same NDA or BLA, either as part of the original application or under a supplement to such application. Further, the approval or licensure of any drug product or biological product must have occurred at least seven or 11 years (as applicable) prior to the selected drug publication date (i.e., the relevant supplement must be at least seven or 11 years old).***

Alternatively, if CMS adopts this overly broad interpretation of the QSSD definition despite the concerns raised below, then PhRMA urges CMS not to adopt its new proposed approach to aggregation of certain fixed-combination products that involve a change in route of administration, which raises significant legal and policy concerns as set forth in section B below. ***Specifically, CMS should finalize 42 C.F.R. § 429.125(b)(4), but without the exception in proposed 42 C.F.R. § 429.125(b)(4)(i).***

A. PhRMA opposes the overbroad interpretation of a QSSD that CMS used for IPAY 2026, 2027 and 2028 and generally proposes to maintain under the Proposed Rule.

The IRA defines a QSSD, in relevant part, as follows:

> (A) DRUG PRODUCTS.—A drug—
>
> > (i) that is *approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act* and is marketed pursuant *to such approval*;
> >
> > (ii) for which, as of the selected drug publication date with respect to such initial price applicability year, *at least 7 years* will have elapsed since the date of *such approval*; and
> >
> > (iii) that is not the listed drug for any drug that is approved and marketed under section 505(j) of such Act.
>
> (B) BIOLOGICAL PRODUCTS.—A biological product—
>
> > (i) that is *licensed under section 351(a) of the Public Health Service Act* and is marketed under section 351 of such Act;

> (ii) for which, as of the selected drug publication date with respect to such initial price applicability year, *at least 11 years* will have elapsed since the date of *such licensure*;
>
> (iii) that is not the reference product for any biological product that is licensed and marketed under section 351(k) of such Act.[41]

Thus, the statute establishes two key requirements for each QSSD:

i. **Approval under an NDA or BLA.** A QSSD must be "approved under section 505(c)" of the FDCA or "licensed under section 351(a)" of the PHSA. At least seven years (for a drug) or 11 years (for a biological) must have elapsed since the date of "such approval," or "such licensure" — both in the singular, referencing a single new drug application (NDA) or biologics license application (BLA). Therefore, each QSSD is limited to drug products or biological products approved under the same NDA or licensed under the same BLA. The terms "drug product" or "biological product" refer to the finished product, including the unique dosage form, strength and route of administration.[42]

ii. **Age Requirement.** For a drug product, the statute requires "at least seven years" to have elapsed from the date of approval to the selected drug publication date. For a biological product, the statute requires "at least 11 years" to have elapsed from the date of approval to the selected drug publication date. Because a drug product or biological product cannot be marketed until it is approved or licensed,[43] the seven or 11 year "age requirement" must be applied to each particular drug product or biological product, whether it was approved under the original NDA/BLA or a supplement to a given NDA or BLA.

Despite these clear Congressional directives, CMS proposes to continue using an overly broad interpretation of a QSSD that impermissibly aggregates drug products and biological products based on their active moiety or active ingredient—neither of which is mentioned in the IRA—and now proposes to add a special, novel rule for certain fixed combinations that is unmoored from the statute.

CMS' approach has concrete consequences. For example, Austedo XR products were approved under a separate NDA in 2023, years after Austedo products were approved in 2017. Nevertheless, CMS aggregated the products based on their shared active moiety. As a result, Austedo XR products were swept into the same QSSD as Austedo products and became eligible for selection for IPAY 2027 based on the approval date of first Austedo NDA, rather than receiving their own independent seven-year period before potential selection. This outcome illustrates the central flaw in CMS' interpretation: by aggregating products approved under different NDAs/BLAs and applying the age requirement based on the earliest

[41] Social Security Act (SSA) § 1192(e)(1) (emphasis added).
[42] *See* e.g., 21 C.F.R. § 314.3, defining "drug product" as "a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients."
[43] *See* FDCA §§ 505(a), 506A(a), (c); PHSA § 351(a)(1); 21 C.F.R. §§ 314.70, 601.12.

approval date, CMS effectively shortens the period Congress specified for selection of drug or biological products. That result is inconsistent with the IRA's requirement that at least seven or eleven years have elapsed since "such approval" or "such licensure" of the NDA or BLA at issue.

Specifically, under the Proposed Rule, "all dosage forms and strengths of the drug with the same active moiety as identified using public sources . . . , and the same NDA holder," constitute the same QSSD. For biological products, the Proposed Rule describes a QSSD as "all dosage forms and strengths of the biological product with the same active ingredient as identified using public sources . . . and the same BLA holder." Additionally, CMS misapplies the age requirement. Consistent with past guidance, CMS states that it will use "the initial date of approval associated with the earliest-approved FDA application belonging to the NDA holder and containing the active moiety" or "earliest-approved FDA application belonging to the BLA holder and containing the active ingredient" "(or in the case of potential [QSSDs] identified under § 429.125(b)(4) [i.e., fixed combinations not subject to the proposed special rule], the distinct combination of active moieties)" to determine whether the respective seven- or 11-year period for QSSD status has elapsed. The statute, however, requires each individual drug product or biological product to meet the age requirement. Moreover, as discussed in subsection I.B, CMS' proposed second statutory interpretation targeted at certain fixed combinations involving a new route of administration raises significant legal and policy issues.

A QSSD must be limited to drug products/biological products that are approved/licensed under a single NDA/BLA.

The terms "active moiety" and "active ingredient" appear nowhere in the QSSD statutory definition (or anywhere in the IRA). Rather, as explained above, the statute unambiguously defines the scope of a QSSD based on an individual NDA or BLA.

The statute's anchor to an NDA or BLA aligns with the fact that Congress authorized FDA to "approve" and "license" drug products and biological products, not their active moieties and active ingredients alone. Moreover, both prongs of the QSSD definition refer to finished products: the subparagraph header for drugs is "[d]rug products," not drug substance or active moiety, and the subparagraph header for biological products similarly refers to "[b]iological products," not active ingredients.

Had Congress intended to define QSSD at the active moiety or active ingredient level, it would have said so in the statute. As demonstrated in an amendment to the FDCA's new chemical entity exclusivity provisions that replaced the term "active ingredient" with "active moiety,"[44] Congress is familiar with both of these terms and knows how to use them when they are intended.[45]

CMS claims that it is "proposing to identify a potential [QSSD] using the specific constituent dosage forms and strengths that are identified as aggregated under the same NDA/BLA holder for the same active moiety/active ingredient, inclusive of products that are marketed under different NDAs/BLAs" "to give full effect to all relevant provisions of the statute, including sections 1192(d)(3)(B), 1192(e),

[44] Pub. L. No. 117-9, § 1(a)(1)(A), 135 Stat. 249 (2021).
[45] *See*, *e.g.*, *Custis v. United States*, 511 U.S. 485, 493 (1994) ("The contrast between § 924(e) and statutes that expressly provide avenues for collateral attacks . . . point[s] strongly to the conclusion that Congress did not intend to permit collateral attacks on prior convictions under § 924(e)."); *Meghrig v. KFC Western, Inc.*, 516 U.S. 479, 485 (1996) ("Congress thus demonstrated in CERCLA that it knew how to provide for the recovery of cleanup costs, and that the language used to define the remedies under RCRA does not provide that remedy.").

1194(e)(1)(D), and 1196(a)(2) of the Act." For the reasons explained below, however, these provisions do not support this proposal:

First, section 1192(d)(3)(B), the "Use of Data" provision, states:

> In determining whether *a qualifying single source drug* satisfies any of the criteria [related to a negotiation-eligible drug and the small biotech exception] the Secretary shall use 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*.[46]

The references to "a qualifying single source drug" and "the drug"—both singular—demonstrate that this provision directs CMS to aggregate data across dosage forms and strengths within an already-identified QSSD. Nothing in section 1192(d)(3)(B) permits or requires CMS to expand the scope of a QSSD to encompass drug products or biological products approved under different NDAs or BLAs. Rather, the provision presupposes the existence of a QSSD and specifies how CMS must evaluate that QSSD for purposes of determining eligibility. The statute makes clear that a QSSD consists of drug products or biological products that meet the applicable age requirement and are approved under a single NDA or BLA, including supplements to that application.

Second, section 1192(e), which defines a QSSD, likewise provides no support for CMS' proposal. As discussed above, that provision ties a QSSD to eligible drug products or biological products approved or licensed under a single NDA or BLA. Nothing in the statutory definition authorizes CMS to combine products approved under different NDAs or BLAs into a single QSSD.

Third, section 1194(e)(1)(D) is similarly inapposite. That provision directs CMS, during the price setting process, to consider, among other information, "applications and approvals under section 505(c) of the [FDCA] or section 351(a) of the [PHSA]" for the drug under consideration. The fact that Congress referred to "applications and approvals" in the plural does not authorize CMS to redefine the statutory scope of a QSSD or to aggregate products approved under different NDAs or BLAs when determining whether a QSSD exists. Rather, Section 1194(e)(1)(D) governs the information CMS may consider after a QSSD has been identified and selected for price setting. It therefore sheds no light on, and provides no authority for altering, the threshold statutory definition of a QSSD set forth in section 1192(e).

Fourth, section 1196(a)(2) likewise does not support CMS' proposal. This provision directs CMS to "apply the maximum fair price [(MFP)] across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." By its plain terms, section 1196(a)(2) addresses the application of an MFP after a drug has already been identified as a selected drug. It ensures that the MFP applies uniformly across the different strengths and dosage forms of that selected drug. Nothing in this provision speaks to, much less expands, the statutory definition of a QSSD or authorizes CMS to aggregate products approved under different NDAs or BLAs for purposes of identifying a QSSD. Indeed, the provision presupposes that the relevant "selected drug" has already been identified in accordance with the statutory criteria. CMS, therefore, cannot rely on section 1196(a)(2), a

[46] SSA § 1192(d)(3)(B) (emphasis added).

provision governing the implementation of an MFP, to rewrite the antecedent definition of a QSSD established by Congress in section 1192(e).

In short, none of the provisions cited by CMS authorizes CMS to depart from the statutory definition of a QSSD by aggregating products approved under different NDAs or BLAs into a single QSSD. Had Congress intended such aggregation, it would have said so expressly. Instead, Congress defined a QSSD by reference to products approved or licensed under a particular NDA or BLA, and CMS must adhere to that definition.

Each drug product or biological product in a QSSD must independently meet the age requirement.

PhRMA opposes CMS' proposal to base the age requirement on the date of approval or licensure associated with the earliest-approved FDA application belonging to the NDA or BLA holder and containing the relevant active moiety or active ingredient (or, in the case of a potential QSSD identified under § 429.125(b)(4), the distinct combination of active moieties/active ingredients). PhRMA also opposes CMS' proposal to base the age requirement for a potential QSSD identified under § 429.125(b)(4)(i) on the initial date of approval or licensure of the earliest-approved FDA application belonging to the NDA or BLA holder and containing the shared active moiety(ies)/active ingredient(s) identified in § 429.125(b)(4)(i). Under these approaches, even a new drug product or biological product (e.g., a new dosage form or strength) approved under a supplemental application after an MFP has been set would be part of the existing QSSD and saddled with its pre-existing MFP. This approach directly conflicts with the statute, which requires that each drug product or biological product independently meet the age requirement. CMS lacks the authority to extend MFPs to drugs and biologics that have not been approved or licensed for the statutorily-specified number of years.

As explained above, the statutory QSSD definition refers back to the number of years (i.e., seven or 11 years) since "such approval" under section 505(c) of the FDCA or section 351(a) of the PHSA. By law, a new drug product or biological product must be approved before it can be marketed. Thus, for each drug product or biological product, the relevant approval date is the date of FDA approval of the original or supplemental NDA/BLA for that drug product or biological product — not the approval date of an older drug product or biological product that happens to have the same active moiety or active ingredient.

Maintaining CMS' current approach will further stifle medical innovation.

Not only is CMS' proposed QSSD definition inconsistent with the statute, if finalized, it would hurt patients by continuing to curb incentives for innovation. Under CMS' approach, once a product containing a novel active ingredient or active moiety has been approved or licensed, incentives for ongoing or new research on drug or biological products with that active ingredient or moiety would sharply decline. No matter how clinically significant the innovation is, the same manufacturer's novel product with a previously approved active moiety or ingredient would be subject to selection for price setting if approved after the seven- or 11-year period for the initial product. Therefore, this approach can broadly cut incentives to invest in a variety of medical advances. For example, the National Pharmaceutical Council has concluded that the price setting program has and will lead to delays in single-indication drug launches, reduce investments in post-approval research for new indications and have a

negative impact on long-term health outcomes.[47] Another study observed, since passage of the IRA, a "35% decline in clinical trial launches for the Medicare-aged population and a 70% decline in funding for early-stage developments in small molecules [that] indicates significant negative impacts on the population the IRA legislation is allegedly designed to aid."[48] Even if a product with a previously approved active moiety or active ingredient were improved in a way that provides a different and meaningful benefit to patients, the improved product would not receive its own seven- or 11-year period (for drugs or biologics, respectively) before potential identification as a QSSD. For example, products with wholly novel delivery systems for previously approved active ingredients that allow for safer, more effective and more accessible treatment, such as in the home, would be discouraged. As noted earlier, such a product could even have an MFP from day one — which suggests that the research to fuel development of the advanced product may never occur. To avoid these disincentives for pharmaceutical innovation that will harm public health, CMS should revise its aggregation methodology to conform to the statute.

B. If CMS adopts its proposed broad interpretation of the QSSD definition, it should nevertheless finalize 42 C.F.R. § 429.125(b)(4) without the exception for certain fixed combinations that enable a new route of administration in proposed § 429.125(b)(4)(i).

With respect to fixed-combination products, CMS should apply a consistent approach for the purposes of identifying QSSDs and should not adopt its proposal to adopt a special rule for certain fixed combinations involving a new route of administration.

Consistent with prior guidance that will remain in place for selected drugs for IPAYs 2026, 2027, and 2028, CMS proposes to generally treat a distinct fixed-combination product as one active moiety, active ingredient, or antigen component for purposes of identifying QSSDs. Specifically, under CMS' proposed rule, "a product containing only one (but not all) of the active moieties, active ingredients, or antigen components that is offered by the same NDA/BLA holder would generally not be aggregated with the formulations of the fixed combination drug and would be considered a separate potential [QSSD]." However, in § 429.125(b)(4)(i) CMS now proposes an unfounded exception: If a fixed-combination product and another product "differ in active moiety(ies), active ingredient(s), or antigen component(s) due to the inclusion of an active moiety, active ingredient, or antigen component that creates a new formulation and enables an alternative route of administration for the co-administered active moiety(ies), active ingredient(s), or antigen component(s), CMS identifies a potential [QSSD] using all dosage forms and strengths of the drug or biological product with the shared active moiety(ies), active ingredient(s), or antigen component(s) and the same NDA/BLA holder."

CMS' approach to fixed-combinations in the Proposed Rule is distinct from the one proposed in the IPAY 2028 Draft Guidance, where CMS considered evaluating whether an active moiety/active ingredient/antigen component was "biologically active against the disease state(s) [for] which the drug is indicated" in determining whether to aggregate fixed-combination product and individual active ingredients or active moieties. CMS rightly declined to finalize this approach for IPAY 2028 and instead

[47] Patterson J., Motyka J., O'Brien J.M. (February 2024). Unintended consequences of the Inflation Reduction Act: clinical development toward subsequent indications. *Am J Manag Care.* Available at: https://pubmed.ncbi.nlm.nih.gov/38381543/
[48] Schulthess D.G. et al. (April 2025). The Inflation Reduction Act's Impact Upon Early-Stage Venture Capital Investments. *Ther Innov Regul Sci.* Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC12181096/

retained the interpretation used in its IPAY 2026 and 2027, in which fixed-combination products are appropriately treated as distinct potential QSSDs from individual active ingredients and active moieties.

Specifically, we agree with the Proposed Rule's abandonment of the approach from the IPAY 2028 Draft Guidance and its focus on "biologically active" ingredients. As PhRMA explained in its comments to that Draft Guidance, this proposed interpretation suffered from numerous flaws, including that the statute does not authorize CMS to consider biological activity of product ingredients or to second-guess FDA's decisions about whether a component is considered active in connection with licensure of a biological product when identifying potential QSSDs. We therefore agree that CMS rightly rejected this approach as discussed in the preamble to the Proposed Rule.

Unfortunately, CMS' new proposal fares no better. CMS asserts that its new proposal is necessary to address a purported "program integrity risk" that manufacturers may seek to avoid selection or application of an MFP by developing fixed-combination products that include an additional ingredient, such as hyaluronidase, to enable an alternative route of administration. CMS fails to identify evidence that manufacturers are developing these fixed combinations for reasons related to IRA selection. CMS acknowledges only a theoretical possibility that manufacturers "may" have incentives to develop such products. The existence of a hypothetical incentive is not and could not be a sufficient basis to disregard the statutory definition of a QSSD or to adopt a policy that treats similarly situated fixed-combination products differently. Nor does CMS have authority to rewrite the statutory framework based on a perceived policy concern that Congress itself did not identify in the IRA. If CMS believes a program integrity risk exists, it may bring that concern to Congress's attention. It may not, however, unilaterally create an extra-statutory solution that alters the scope of the QSSD definition established by Congress.

Moreover, CMS overlooks the legitimate scientific, clinical and practical reasons manufacturers may develop intravenous single active ingredient and subcutaneous fixed combination products sequentially. In many cases, an intravenous single active ingredient product can be developed and brought to patients more quickly, allowing patients to gain access to a novel therapy while additional research is conducted to develop a subcutaneous fixed combination product. Developing a subcutaneous fixed combination product, particularly one incorporating an additional component such as hyaluronidase, may require substantial additional research to address distinct scientific, quality and clinical considerations. By treating a later-developed subcutaneous fixed-combination product as part of the same QSSD as an earlier intravenous single active ingredient product, CMS risks reducing incentives to invest in these clinically meaningful improvements. Such products can provide important benefits to patients and providers, including shorter administration times, reduced treatment burden, greater convenience and the ability to receive treatment in alternative settings, including the home.

Furthermore, the products at issue do not necessarily involve the combination of previously approved active ingredients. In some instances, an active ingredient used to enable subcutaneous administration is itself a novel agent that was not previously approved in the United States. This fact further undercuts the premise that such products should be treated as the same QSSD to the single ingredient intravenous product for purposes of the Program.

Notably, some of the products that appear to have prompted CMS' concerns—i.e., products incorporating hyaluronidase to facilitate subcutaneous administration—reflect innovations that were approved before

enactment of the IRA. Indeed, CMS even acknowledges "incentives for pharmaceutical manufacturers to develop new formulations like the ones we propose to address in this policy *long predate* the . . . Program."

More fundamentally, rather than protecting program integrity, the proposal risks discouraging precisely the type of patient-centered innovation that has produced meaningful clinical benefits for patients. Products that enable alternative routes of administration can reduce treatment burden, improve convenience, decrease time spent in clinical settings, and expand patient access to therapies by allowing treatment in less resource-intensive settings. Treating such innovations as though they were merely attempts to circumvent the Program fails to recognize the substantial investment, clinical development, and regulatory review required to bring these products to market. CMS should not adopt a policy that could chill the development of innovative products that serve legitimate patient-care objectives and improve patient outcomes.

The proposal also raises substantial legal concerns. First, there is no statutory basis for CMS' proposed approach. As discussed above, Congress directed CMS to identify QSSDs based on approved drug products and licensed biological products and the applicable NDA or BLA. Nothing in the statutory definition of a QSSD authorizes CMS to disregard the existence of a distinct fixed-combination product because an additional active moiety, active ingredient, or antigen component "creates a new formulation and enables an alternative route of administration." Indeed, the statute says nothing about routes of administration, illustrating how CMS' proposed special rule for these fixed combinations is unmoored from the statute. Under the proposed exception, CMS would treat certain fixed-combination products differently from all other fixed-combination products based on criteria that appear nowhere in the statute. Nor can CMS substitute its policy judgment for the framework enacted by Congress. If Congress had intended CMS to aggregate fixed-combination products with products containing only a subset of their active moieties, active ingredients, or antigen components whenever the additional active component facilitated a different route of administration, it would have said so expressly. Instead, Congress adopted a definition of QSSD that turns on approved drug and biological products and the relevant NDA or BLA, not on CMS' assessment of the function performed by a particular ingredient or changes in route of administration. Accordingly, CMS' proposed fixed-combination exception exceeds its statutory authority and should not be finalized.

The arbitrariness of CMS' approach is illustrated by the fact that the agency proposes aggregating products that add a new active moiety or active ingredient and enable a different route of administration, while continuing to treat as separate QSSDs products that add a new active moiety or active ingredient *without* enabling a new route of administration. The statute does not identify route of administration as a relevant criterion for defining a QSSD, and CMS does not adequately explain why that feature should be dispositive. Indeed, CMS never explains why the larger change—adding a new active ingredient and changing the route of administration—should result in aggregation, while other fixed-combination products containing different active ingredients remain distinct QSSDs. Nor is the answer to expand the proposed exception in § 429.125(b)(4)(i) to all fixed-combination products. Indeed, the Proposed Rule recognizes the importance of the proposed general rule. Rather, CMS should abandon the exception

altogether because the statute provides no basis for treating fixed-combination products differently based on whether an additional active ingredient enables an alternative route of administration.[49]

Moreover, CMS' reliance on sections 1192(d)(3)(B) and 1196(a)(2) does not resolve the problem. CMS asserts that the exception in proposed § 429.125(b)(4)(i) "would effectuate" (1) section 1192(d)(3)(B), which, as noted above, directs CMS to aggregate data "across dosage forms and strengths of the drug, including new formulations of the drug," and (2) section 1196(a)(2), which directs CMS to apply the MFP "across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." As explained, however, those provisions presuppose that CMS has already determined which products belong to the same QSSD. Section 1192(d)(3)(B) does not define the scope of a QSSD; rather, it instructs CMS how to evaluate a negotiation-eligible drug and apply the small biotech exception once a QSSD is identified by requiring CMS to aggregate data across the dosage forms and strengths of that drug. Similarly, section 1196(a)(2) governs how the MFP applies after a selected drug has been identified. Neither provision answers the antecedent question of whether products with different active moieties, active ingredients, or antigen components should be treated as the same QSSD in the first place. Nor do they authorize CMS to aggregate products based on whether one component enables an alternative route of administration.

Second, CMS has not articulated a scientifically or legally coherent basis for the proposed "narrowly tailored" exception from its general fixed combination aggregation rule and for departing from FDA's framework for such products. CMS' general rule for identifying potential QSSDs using all dosage forms and strengths of the drug or biological product with the same distinct combination of active moieties, active ingredients, or antigen components reflects the single, best meaning of the statute and should govern all fixed combinations. Nevertheless, despite defining "fixed-combination drug" as "having the meaning set forth in 21 C.F.R. § 300.50," the proposed "narrowly tailored" exception departs from FDA's longstanding regulatory framework governing such products. FDA's regulation at 21 C.F.R. § 300.50 provides that "[t]wo or more drugs may be combined in a single dosage form when each component makes a contribution to the claimed effects" and expressly contemplates circumstances in which a component is added to enhance the safety or effectiveness of another component. Under that framework, an active ingredient such as hyaluronidase is no less an active ingredient because it also enables an alternative route of administration of a formulated active ingredient. Indeed, FDA has licensed biological products containing hyaluronidase as the sole active ingredient. Although CMS acknowledges commenters' concerns that the proposal "would not align with how FDA regulates and reviews" fixed-combination products, CMS dismisses those concerns without meaningfully addressing them. FDA's framework reflects a longstanding scientific and regulatory understanding that active ingredients may contribute to a product's safety and effectiveness in multiple ways; yet CMS offers no reasoned basis for departing from that framework, particularly when it purports to rely on FDA's definition of a fixed-dose combination drug in 21 C.F.R. § 300.50 to define "fixed-combination product."

[49] *See Bracco v. Shalala*, 963 F. Supp. 20 (D.D.C. 1997) ("The Court concludes that plaintiffs are likely to succeed on the merits of their [Administrative Procedure Act (APA)] claim that the FDA has failed to treat similarly situated products in the same fashion and that such conduct is arbitrary and capricious."). The APA requires a court to set aside agency actions, findings, and conclusions found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A).

This unexplained departure is particularly significant because the IRA itself defines QSSDs by reference to drugs approved under section 505(c) of the FDCA and biological products licensed under section 351(a) of the PHSA. FDA's identification of the relevant drug or biological product is therefore directly relevant to the QSSD inquiry. Yet CMS proposes treating certain FDA-approved fixed-combination products as mere new formulations of another product while continuing to treat other FDA-approved fixed-combination products as distinct QSSDs. CMS offers no principled explanation for this distinction, which creates an arbitrary disconnect between the FDA approval framework expressly referenced in the IRA and the QSSD framework CMS proposes to implement. Moreover, as explained above, CMS lacks statutory authority to adopt this special rule; the general rule for identifying potential QSSDs for fixed combinations in 42 C.F.R. § 429.125(b)(4) reflects the single, best meaning of the statute and should govern all fixed combinations.

Manufacturers have long relied on FDA's fixed-combination drug framework when making research, development, and commercialization decisions. Under that framework, sponsors can expect that a product containing multiple active ingredients that each contribute to the product's claimed effects will be licensed as a distinct fixed-combination product. CMS' proposal would introduce substantial uncertainty by subjecting certain FDA-approved fixed-combination products to a different standard under the Negotiation Program based on CMS' assessment of the role played by a particular active ingredient.

Third, CMS has failed to provide a reasoned explanation for abandoning its own established interpretation of QSSD with respect to fixed combinations.

An agency must provide a reasoned explanation for disregarding "facts and circumstances that underlay or were engendered by the prior policy."[50] CMS has not done so here. Nor has CMS identified any authority that would permit it to override FDA's scientific judgments regarding active ingredients and fixed-combination products. By inappropriately effectively recharacterizing certain FDA-approved fixed-combination products as merely new formulations of another product for purposes of identifying QSSDs, CMS creates regulatory uncertainty for manufacturers and risks creating unnecessary conflict with FDA's regulatory framework governing the same products.

Fourth, the proposed rule conflicts with the holding of *Loper Bright* that courts must identify and apply the single, best meaning of a statute. In *Loper Bright*, the Supreme Court made clear that agencies are not entitled to deference when interpreting statutes and that the governing question is the statute's single, best meaning. Yet CMS does not contend that the IRA's text is best read to require aggregation of fixed-combination products with products containing only a subset of their active moieties, active ingredients, or antigen components when an additional component enables an alternative route of administration. Nor does CMS explain how such a distinction can be reconciled with the statute's focus on FDA-approved drug products and biological products and the relevant NDA or BLA. Indeed, CMS agrees that generally fixed-combination products should be treated similarly under § 429.125(b)(4). CMS relies primarily on policy concerns regarding perceived "program integrity" risks to create an exception for certain products it disfavors. But policy concerns cannot substitute for statutory authority. If the statute's purported best reading does not authorize CMS' proposed fixed-combination exception, CMS may not adopt that policy simply because it views the outcome as preferable.

[50] *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 516 (2009).

Instead, the special exception in proposed § 429.125(b)(4)(i) reflects that CMS has not adopted the *single*, best meaning of the statute. The single, best interpretation is the general rule in proposed 42 C.F.R. § 429.125(b)(4), which should be the universal rule. Instead, CMS has crafted a second interpretation of the QSSD definition that is unique to these fixed combinations. Specifically, for IPAYs 2026 through 2028, CMS consistently treated fixed-combination products as distinct potential QSSDs from products containing only a subset of their active moieties, active ingredients, or antigen components. CMS now proposes a materially different approach for certain fixed-combination products but does not identify any intervening statutory change, newly discovered fact, or textual analysis demonstrating that its prior interpretation was incorrect. Rather than showing that the proposed approach reflects the statute's single, best meaning, because it cannot, CMS instead advances a different policy judgment regarding which products should be selected. Under *Loper Bright*, however, the relevant question is not which approach CMS prefers as a matter of policy, but which approach is most faithful to the statute enacted by Congress. CMS' proposed interpretation fails to satisfy that standard.

II. Biosimilars "Pause" (§ 429.110)

PhRMA urges CMS to implement the biosimilars "pause" provision in section 1192(f) in a way that promotes predictability for biologic and biosimilar manufacturers in the marketplace. Congress has enacted a "Special Rule"[51] enabling certain biosimilar manufacturers to obtain a "pause" before the reference product is selected for MFP price setting to allow time for the biosimilar product to secure approval and begin marketing.[52] The statute provides for an initial 1-year "pause" if CMS determines there is a "high likelihood" that a biosimilar will be "licensed and marketed" before the date that is two years after the selected drug publication date with respect to the IPAY.[53] Further, the statute requires CMS to "delay the inclusion of" a reference product on the list of selected drugs for a second 1-year period if the biosimilar product has not been licensed and marketed during the initial 1-year period and, in response to a request timely made by a biosimilar manufacturer, CMS determines that:

> (1) there remains a "high likelihood . . . that such biosimilar biological product . . . will be licensed and marketed . . . before the date that is two years after the selected drug publication date for which such biological product" would have been a selected drug, and
>
> (2) "on the basis of clear and convincing evidence," the biosimilar manufacturer "has made a significant amount of progress. . . towards both such licensure and the marketing of such biosimilar biological product . . . since the receipt by the Secretary" of the request for an initial 1-year pause.[54]

In this context, it is critical that CMS implements the "pause" provision in as predictable and flexible a manner as possible. In this regard, we are concerned by the brief and inflexible 30-day window CMS anticipates for submission on initial delay requests. We also urge CMS to revise its approach to

[51] Pub. L. 117-169 § 1102, 136 Stat. 1818, 1854. (August 2022). Available at: https://www.congress.gov/117/plaws/publ169/PLAW-117publ169.pdf
[52] SSA § 1192(f)(1)(A).
[53] SSA § 1192(f)(2)(A).
[54] SSA § 1192(f)(2)(B).

determining whether there is a "high likelihood" that a biosimilar product will be licensed and marketed during the relevant time period by adhering more closely to the statute and providing additional clarity and flexibility. CMS should also provide greater clarity and details regarding what constitutes "clear and convincing evidence" of a "significant amount of progress" in support of an additional delay request. We provide factors that should guide CMS' determination that there is "clear and convincing evidence" of a "significant amount of progress" towards licensure and marketing of the biosimilar product.

Predictable and flexible implementation of the "pause" is required to maintain a robust and competitive U.S. market through biosimilar competition.

Congress created a carefully balanced system through the Biologics Price Competition and Innovation Act (BPCIA) to encourage competition in the marketplace between reference biologics and biosimilars, while maintaining incentives for continued innovation. Since the introduction of the first biosimilar in 2015, a total of 66 biosimilars have launched to compete against 18 brand biologic products leading to a total of $56.2 billion in savings.[55,56] The introduction of biosimilar competition into the biologics market has led to dramatically lower prices not only for biosimilars, but also for reference products.[57] One study examining average sales prices in Medicare since 2015 found brand biologic prices dropped ten to 13 percent for *each* additional biosimilar competitor, with some brand biologics competing with as many as six biosimilars at that time.[58,59]

The IRA jeopardizes this carefully constructed balance by imposing significant burdens on biosimilar manufacturers seeking to enter the market. The timeframes for MFP price setting are in many cases well before it is feasible for a biosimilar to come to market, creating a significant disincentive for manufacturers to invest in these cost-saving alternatives. The processes necessary to bring a biosimilar product to market can be complex, and there are many steps that are not solely in control of the biosimilar sponsor, including FDA review or timelines for patent litigation under the BPCIA's "patent dance" framework. Despite this complexity, the statutory "pause" provisions set rigid time requirements for completion of these activities. The fact that reference biologics may be selected for MFP price setting before the biosimilar may even be eligible for licensure only exacerbates the timing issues. Even though biosimilars may not be approved until 12 years after the first licensure of a reference product,[60] the IRA allows selection of the reference product for MFP-setting after only 11 years.

CMS should provide a longer window of time for submitting initial delay requests and notice to the reference product manufacturer.

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[55] Cencora. (May 2026). U.S. Biosimilars Landscape. Available at: https://go.cencora.com/biosimilars-pipeline-report
[56] Association for Accessible Medicines. (September 2025). 2025 U.S. Generic & Biosimilar Medicines Savings Report. Available at: https://accessiblemeds.org/wp-content/uploads/2025/09/AAM-2025-Generic-Biosimilar-Medicines-Savings-Report-WEB.pdf
[57] Xcenda. (July 2022). Biosimilars are Lowering Costs in the Medicare Part B and Across the Healthcare System Overall. Available at: https://www.xcenda.com/-/media/assets/xcenda/english/content-assets/white-papers-issue-briefs-studies-pdf/xcenda_biosimilar_trends_issue_one_july2022.pdf
[58] Jofre-Bonet M. et al. (May 2025). The Price Effects of Biosimilars in the United States. *Value in Health*. Available at: https://www.valueinhealthjournal.com/article/S1098-3015(25)00086-5/abstract?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1098301525000865%3Fshowall%3Dtrue
[59] PhRMA. (October 2021). The U.S. Market for Biosimilars and Biologics Medicines. Available at: https://www.phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/A-C/PhRMA---Biosimilars-Market-Multi-Pager_v11.pdf
[60] PHSA § 351(k)(7)(A).

CMS explains that it is proposing revisions to a currently approved information collection for a manufacturer to submit an Initial Delay Request, for a 60-day public comment period concurrently with the Proposed Rule.[61] The Information Collection Request (ICR) explains, however, consistent with prior guidance, that CMS anticipates a 30-day window for submission of Initial Delay Requests.[62] We are concerned that biosimilar manufacturers cannot predict when OMB may approve the ICR and that 30 days is an inadequate time period to prepare and submit such requests. The lack of notice and brevity of the submission window offer neither the predictability nor flexibility needed to implement the biosimilar pause effectively.

In the interests of transparency, CMS should provide notice to the reference product manufacturer when a biosimilar manufacturer submits a "pause" request identifying the reference product. Because CMS' determination may directly affect the timing of selection of the reference product, the reference product manufacturer has a significant interest in the proceeding and should receive timely notice that a request has been submitted. Providing such notice would promote predictability for all affected parties and would not impose a meaningful administrative burden on CMS.

CMS' interpretation of the "high likelihood" requirement is untethered from the statute, unworkably vague, and overly rigid.

The statute directs CMS to determine that there is a "high likelihood" the biosimilar product will be licensed and marketed if it finds that FDA has accepted for review or has approved a biosimilar application, and information submitted by the biosimilar manufacturer "provides clear and convincing evidence that such biosimilar biological product will," within the specified time period, "be marketed."[63] Specifically, the statute provides that CMS will consider the following information in determining whether there is such a "high likelihood":

- All agreements related to the biosimilar product filed with the Federal Trade Commission (FTC) or Assistant Attorney General (DOJ) pursuant to section 1112(a) and (c) of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA);
- To the extent available, the manufacturing schedule for the biosimilar product submitted to FDA during its review of the BLA; and
- To the extent available, certain disclosures by the biosimilar manufacturer that pertain to the marketing of the biosimilar product and that are made in certain filings with the Securities and Exchange Commission (SEC) or in comparable documentation distributed to the shareholders of privately held companies.[64]

As explained above, under *Loper Bright*, an agency is required to apply the "single, best meaning" of a statute.[65] Also as noted above, the President issued a memorandum on April 9, 2025, prioritizing the review and repeal pursuant to Executive Order 14219 of existing regulations that are unlawful under

[61] 91 Fed. Reg. 36247.
[62] Reginfo.gov. (June 2026). PRA ICR Documents at 4. Available at: https://www.reginfo.gov/public/do/PRAViewDocument?ref_nbr=202606-0938-004
[63] SSA § 1192(f)(3).
[64] SSA § 1192(f)(3)(B).
[65] 144 S. Ct. 2244, 2266 (2024).

Loper Bright.[66] CMS has not implemented the statutory provisions governing the information to be used to make a "high likelihood" determination in a manner that represents the single, best meaning of the statute. The approach described in the Proposed Rule is inconsistent with the statute and is burdensome.

For example, CMS maintains under proposed § 429.110(d) that, for CMS to determine that there is a "high likelihood" that a biosimilar biological product will be licensed and marketed within the applicable statutory timeframe, "[b]y no later than a date to be specified by CMS, which will be in *January* in the calendar year of the selected drug publication date for the initial price applicability year for which the Biosimilar Manufacturer requests the delay," the biosimilar application must have "been either (i) approved by the FDA; or (ii) accepted for review by FDA."[67] CMS' choice of January does not represent the single, best meaning of the statute. Given the rigid timelines associated with the statutory "pause" and the fact that biologics may be selected for MFP price setting before the biosimilar may even be eligible for licensure, CMS should allow the biosimilar manufacturer to submit information indicating that its application for licensure will be accepted for review or approved by FDA by the date of selection. CMS should also consider providing at least one quarter of advance notice to manufacturers of drugs anticipated for selection and providing biosimilar manufacturers the opportunity to inquire if a particular reference biologic is among the drugs anticipated for selection.

With respect to CMS' evaluation of the "high likelihood" of marketing, PhRMA has significant concerns with CMS expectations that the above information submitted by the biosimilar manufacturer "demonstrates both: (1) that patents *related to* the Reference Drug are unlikely to prevent the Biosimilar from being marketed; and (2) that the Biosimilar Manufacturer will be operationally ready to market the Biosimilar."[68] CMS proposes that it will consider the first requirement met if (A) "there will be no unexpired patents relating to the reference product included in the Reference Drug that are applicable to the Biosimilar"; (B) "one or more court decisions or decisions by the United States Patent and Trademark Office (USPTO)'s Patent Trial and Appeal Board (PTAB) establish the invalidity, unenforceability, or non-infringement of any potentially applicable unexpired patents relating to the reference product included in the Reference Drug that a patent holder asserted was applicable to the Biosimilar"; or (C) "neither a court nor PTAB has adversely ruled against the Biosimilar Manufacturer's patent assertion(s) pertaining to unexpired patent(s) relating to the reference product included in the Reference Drug applicable to the Biosimilar, and the Biosimilar Manufacturer has publicly announced a precise launch date for the Biosimilar that is both a calendar date before the High Likelihood Deadline and is not contingent on the outcome of pending litigation;" or "(D) "Biosimilar Manufacturer has a signed agreement with the Reference Manufacturer that permits the Biosimilar Manufacturer to market the Biosimilar before the High Likelihood Deadline, without improper constraints on the Biosimilar Manufacturer."[69]

With respect to the *first* requirement (i.e., "that patents *related to* the Reference Drug are unlikely to prevent the Biosimilar from being marketed"), it is unclear which patents CMS considers to be "related to" the reference product. We urge CMS to clarify or eliminate the first requirement, as it unnecessarily

[66] White House. (April 2025). Presidential Actions, Directing the Repeal of Unlawful Regulations. Available at: https://www.whitehouse.gov/presidential-actions/2025/04/directing-the-repeal-of-unlawful-regulations/
[67] Proposed 42 C.F.R. § 429.110(d).
[68] 91 Fed. Reg. at 46249 (emphasis added). Proposed § 429.110(d)(2).
[69] 91 Fed. Reg. 36249; Proposed 42 C.F.R.§ 429.110(d)(2)(i)(A)-(D).

limits the availability of the "pause." If CMS retains this factor in the Final Rule, PhRMA supports CMS' proposal to consider publicly announced biosimilar launch dates as evidence that patents are unlikely to prevent timely marketing of a biosimilar product. Public-facing statements regarding expected launch timing can provide useful evidence of a biosimilar manufacturer's assessment of the remaining patent and regulatory barriers to entry. CMS should not limit consideration of such statements to the specific circumstances set forth in the Proposed Rule, however.[70] Rather, CMS should retain flexibility to consider other public-facing statements regarding anticipated market entry as relevant evidence in determining whether there is a high likelihood that the biosimilar will be marketed before the "High Likelihood Deadline." More generally, if CMS retains the first requirement, CMS should consider additional or alternative evidence in determining whether patents related to the reference product are unlikely to prevent the biosimilar from being marketed before the "High Likelihood Deadline." CMS should afford biosimilar manufacturers flexibility to determine, on a case-by-case basis, the types of evidence most appropriate to demonstrate that patents are unlikely to prevent such marketing.

With respect to the ***second*** requirement (i.e., "that the Biosimilar Manufacturer will be operationally ready to market the Biosimilar"), the term "operationally ready" is vague and lacks clear parameters. CMS provides only a limited example — "information regarding the operational preparations and/or other steps to market and/or produce the Biosimilar" disclosed in the "Management's Discussion and Analysis (MD&A)" section or another appropriate section of a Form 10-K — but does not explain what other evidence may be sufficient to satisfy this standard.[71] PhRMA is concerned that CMS will implement this language narrowly, to the detriment of biosimilar development. A rigid requirement that the biosimilar demonstrate both showings also undermines the flexibility necessary to avoid undermining the delicate balance Congress established through the BPCIA.

More fundamentally, the Proposed Rule indicates that CMS will evaluate whether there is a high likelihood of *bona fide marketing*, rather than whether there is a high likelihood that the biosimilar product will be *marketed* within the statutory timeframe.[72] The use of the extra-statutory "bona fide" qualifier in this setting will restrict availability of the "pause" and create uncertainty about when it will be available because the statute requires CMS to assess only whether there is a high likelihood that the biosimilar product will be marketed within the applicable timeframe, not whether such marketing satisfies an additional "bona fide" standard. Likewise, the Proposed Rule indicates that CMS may deny the "pause" based on "improper constraints" not mentioned in the statute—i.e., the provisions stating that the "pause" is unavailable where the biosimilar manufacturer and the reference product manufacturer are the same or treated as such and where these parties entered into an agreement that requires or incentivizes the biosimilar manufacturer to submit a "pause" request or that "directly or indirectly" restricts the quantity

[70] That is, "neither a court nor PTAB has adversely ruled against the Biosimilar Manufacturer's patent assertion(s) pertaining to unexpired patent(s) relating to the reference product included in the Reference Drug applicable to the Biosimilar, and the Biosimilar Manufacturer has publicly announced a precise launch date for the Biosimilar that is both a calendar date before the High Likelihood Deadline and is not contingent on the outcome of pending litigation." *See* 91 Fed. Reg. 36249; Proposed 42 C.F.R.§ 429.110(d)(2)(i)(C).

[71] 91 Fed. Reg. at 36,250.

[72] 91 Fed. Reg. at 36,246 ("Proposed § 429.110(b) through (f) address the requirements for a Biosimilar Manufacturer to submit a Biosimilar Delay Request and for CMS to determine if the inclusion of the Reference Drug on the selected drug list should be delayed due to such Biosimilar Delay Request. As set forth in proposed § 429.110(a), for purposes of the provisions at proposed § 429.110 and in our discussion of this section herein, all references to 'marketed' or 'marketing' mean Bona Fide Marketing as defined in proposed § 429.20 and set forth at proposed § 429.130(a).").

of the biosimilar sold in the United States. Specifically, CMS states that it will consider "an improper constraint" to "include[], but is not [be] limited to," these scenarios.[73] CMS does not provide additional insight into what extra-statutory "improper constraints" it references. This interpretation creates additional uncertainty regarding whether a biosimilar delay request will or will not be granted. It also raises concerns regarding fair notice and the potential retroactive application of criteria that manufacturers could not reasonably have anticipated when entering into such agreements.

To give the statute its single, best meaning and to implement an approach that is least burdensome, PhRMA urges CMS to permit submission of additional information and documents by any person or obtained by CMS from any other source for CMS to consider in making a "high likelihood" determination. This approach enables CMS to base its determination on the most comprehensive body of evidence and thus give the statute its single, best meaning. PhRMA appreciates that CMS recognizes the relevance of certain public disclosures, such SEC filings and comparable shareholder communications.[74] However, CMS should clarify that in addition to the examples identified in the Proposed Rule, it may consider other publicly available information, including press releases, investor presentations, earnings-call materials, and similar public communications, as evidence that the biosimilar was accepted for review or approved by FDA, of the status of the biosimilar's clinical studies, and of the expected time to market. Much of the information necessary to make a "high likelihood" determination is available in readily accessible public sources and should not necessitate a burdensome submission by the biosimilar manufacturer.

PhRMA recognizes CMS' statement that evidence of operational readiness includes "information regarding the operational preparations and/or other steps to market and/or produce the Biosimilar under 'MD&A' or another section, as appropriate, in a Form 10-K."[75] PhRMA also appreciates CMS' addition of two examples of evidence that may help support a high likelihood determination: (1) the biosimilar manufacturer's Form 10-K lists a signed agreement with the reference product sponsor, along with a copy of the agreement if required, and (2) the biosimilar manufacturer's Form 10-K reports no adverse patent actions from a court or PTAB and "the Biosimilar Manufacturer publicly announced a precise launch date for the Biosimilar by a calendar date prior to the High Likelihood Deadline."[76] These statements are qualified, however, because CMS states that the examples are "illustrative but alone may not always constitute 'clear and convincing evidence' of a high likelihood of being marketed."[77]

We recommend that CMS revise this content to state that it will find a "high likelihood" of marketing if, absent definitive evidence of an inability to come to market based on the manufacturing schedule, the biosimilar manufacturer meets either of the following criteria:

1. Agreements filed with the FTC/DOJ do not bar the biosimilar manufacturer from marketing the biosimilar product before the end of the relevant period; or

[73] 91 Fed. Reg. at 36,249; *see also* Proposed 42 C.F.R. § 429.110(d)(2)(i)(D).
[74] 91 Fed. Reg. at 36,250.
[75] *Id.*
[76] 91 Fed. Reg. at 36,250.
[77] 91 Fed. Reg. at 36,250.

2. The investor disclosures indicate plans to market, or the manufacturing schedule submitted to FDA for the biosimilar product indicates that commercial lots of the biosimilar product are expected to be produced, before the end of the relevant period.

Consistent with the statute, evidence from *either* category should be sufficient absent contrary evidence demonstrating that the biosimilar is unlikely to be marketed within the relevant period. These statutory criteria are directly tied to the information that the biosimilar manufacturer is required to submit under section 1192(f)(1)(B)(ii). Moreover, allowing the biosimilar manufacturer to satisfy *either* showing provides necessary flexibility to prevent the IRA from jeopardizing biosimilar development.

If CMS has remaining questions about the likelihood of marketing, CMS could also consider the following additional criteria:

- The biosimilar manufacturer has not stated in its disclosures to investors or in filings to the SEC, such as Forms 10-K or 10-Q, that it will not market the biosimilar product before the end of the relevant period;
- The biosimilar manufacturer has not withdrawn its BLA;
- The biosimilar manufacturer is not in arrears for any user fees due under section 744H of the FDCA for the biosimilar application;
- No manufacturing facility where the biosimilar is made, processed, etc., has a classification of Official Action Indicated;
- No clinical trial protocol amendments have been filed that would delay enrollment completion dates and subsequent biosimilar marketing beyond the pause period.

CMS should undertake a predictable and flexible approach toward evaluating requests for the second one-year pause.

If an initial "pause" is granted, then for purposes of assessing whether the requirements for a second 1-year pause have been met, the statute requires CMS to determine, on the basis of "clear and convincing evidence," whether a biosimilar manufacturer has made a "significant amount of progress" toward "licensure" and "marketing." This re-evaluation is to be based on the following sources of information:

All agreements related to the biosimilar product filed with the FTC/DOJ pursuant to section 1112(a) and (c) of the MMA; and

Any additional information and documents submitted by the biosimilar manufacturer in response to a request from CMS.[78]

In the proposed rule, CMS has provided a similar high-level description as in the IPAY 2028 guidance regarding the information it will consider in determining whether a biosimilar applicant has made a "significant amount of progress," continuing to rely on a "holistic review" of the documentation submitted.[79] CMS explains that it will "consider if the Biosimilar Manufacturer can demonstrate affirmative progress towards being operationally ready to market the Biosimilar" and will "consider the Biosimilar Manufacturer's progress on the actions, activities, and milestones that are typical of the normal

[78] SSA § 1192(f)(2)(B)(i)(II).
[79] 91 Fed. Reg. at 36,251.

course of business leading up to the marketing of a drug since the successful Initial Delay Request submission for the Biosimilar evidenced in any updates or supplements to the documents" specified in section 1192(f)(1)(B)(ii)(III).[80] These general descriptions lack specificity and thus do not provide sufficient notice of the types of evidence CMS may consider in making a "significant amount of progress" determination.[81] As noted above, CMS provides "information regarding the operational preparations and/or other steps to market and/or produce the Biosimilar under 'MD&A' or another section, as appropriate, in a Form 10-K" as "one example of evidence that could potentially demonstrate that the Biosimilar Manufacturer is operationally ready;"[82] however, it remains unclear what CMS considers to be "operationally ready" or "actions, activities, and milestones that are typical of the normal course of business leading up to the marketing of a drug."[83] The vagueness of these evidentiary standards will not lead to predictable implementation of the biosimilar pause. We recommend clarifying these points.

We maintain that CMS' analysis of an additional delay request should be both predictable and flexible. To that end, CMS should simply seek attestation by the biosimilar manufacturer that it has made progress toward marketing to determine whether to grant a second-year pause. To the extent CMS makes a further inquiry, it should be limited to definitive evidence of an inability to come to market and absent such definitive evidence of an inability to come to market, CMS should find a "significant amount of progress" if any of the criteria below are met:

1. If the biosimilar application was pending upon review during the first year of the pause:
    a. FDA has since approved the application;
    b. The first cycle of review remains ongoing, i.e., FDA's user fee goal date for action on the application has not yet occurred; or
    c. FDA has issued a complete response letter to the biosimilar manufacturer for the BLA and, as of the time that CMS is assessing eligibility for the second 1-year pause, the biosimilar manufacturer has resubmitted the BLA; or
2. The biosimilar manufacturer's investor disclosures indicate plans to market before the end of the relevant period;
3. The manufacturing schedule submitted to FDA for the biosimilar product indicates that commercial lots of the biosimilar product are expected to be produced before the end of the relevant period; or
4. Agreements filed with the FTC/DOJ do not bar the biosimilar manufacturer from marketing the biosimilar product before the end of the relevant period.

If CMS has remaining questions about the likelihood of marketing, CMS could also consider the following additional criteria:

- The biosimilar manufacturer has not stated in its disclosures to investors that it will not market the biosimilar product before the end of the relevant period;

[80] 91 Fed. Reg. at 36,251.
[81] 91 Fed. Reg. at 36,251; Proposed 42 C.F.R. § 429.110(e)(3).
[82] 91 Fed. Reg. at 36,250.
[83] "Rule of law principles require that parties have fair notice and an opportunity to conform their behavior to legal rules." *Circus Circus Casinos, Inc. v. NLRB*, 961 F.3d 469, 476 (D.C. Cir. 2020).

- The biosimilar manufacturer has not withdrawn its BLA;
- The biosimilar manufacturer is not in arrears for any user fees due under section 744H of the FDCA for the biosimilar application; and
- No manufacturing facility where the biosimilar is made, processed, etc., has a classification of Official Action Indicated.

III. "Bona Fide Marketing" (§ 429.130(a))

PhRMA opposes CMS' extra-statutory concept of "Bona Fide Marketing."[84] In relevant part, section 1192(e)(1) of the SSA defines a QSSD as a drug product "that is not the listed drug for any [generic] drug that is approved *and marketed* under section 505(j)" of the FDCA and a biological product "that is not the reference product for any [biosimilar] biological product that is licensed *and marketed* under section 351(k)" of the PHSA.[85] Similarly, section 1192(c) provides that a product ceases to be a "selected drug" beginning before the first year that begins at least nine months after the date on which the Secretary determines at least one generic drug or biosimilar biological product "is approved or licensed (as applicable)" and "is *marketed* pursuant to such approval or licensure."[86]

Nonetheless, the Proposed Rule states that CMS will "conduct a holistic inquiry based on the totality of the circumstances when evaluating whether the manufacturer(s) of any approved generic drug(s) or licensed biosimilar(s) is or are engaged in *Bona Fide Marketing* of that generic drug or biosimilar."[87] The Proposed Rule further explains that "when evaluating whether a generic drug or biosimilar for a selected drug is subject to Bona Fide Marketing for the purposes of determining if a selected drug ceases to be a selected drug" CMS will "implement the same approach that we propose for evaluating whether a generic drug or biosimilar for a potential [QSSD] is subject to *Bona Fide Marketing*."[88] Moreover, even after CMS determines that a potential QSSD will not be considered a QSSD or that a selected drug has ceased to be a selected drug, CMS proposes "monitor[ing] that the approved generic drug or licensed biosimilar continues to be subject to *Bona Fide Marketing*."[89]

The addition of the term "Bona Fide" adds an extra-statutory limitation and is at odds with the ordinary meaning of "marketed." CMS' approach also is inconsistent with other provisions of the IRA, where Congress expressly imposed volume-based requirements for marketing purposes. Finally, the statute does not permit CMS to monitor for "Bona Fide Marketing" *after* it determines that a product is not a QSSD or has ceased to be a selected drug or even vaguely contemplate such a monitoring program.

The statute does not allow for imposition of CMS' "Bona Fide" qualifier.

As noted, CMS is obligated under *Loper Bright*[90] and the President's April 9, 2025 memorandum[91] to adopt the single, best meaning of the IRA and withdraw any interpretation that conflicts with that single,

[84] Proposed 42 C.F.R. § 429.130.
[85] SSA § 1192(e)(1)(A)(iii) & (B)(iii) (emphasis added).
[86] SSA § 1192(c)(1) (emphasis added).
[87] 91 Fed. Reg. at 36,264 (emphasis added); Proposed 42 C.F.R. §§ 429.20, 429.130.
[88] *Id.* at 36265 (emphasis added); Proposed 42 C.F.R. § 429.135(a).
[89] *Id.* (emphasis added); Proposed 42 C.F.R. § 429.130(a).
[90] *Loper Bright*, 144 S. Ct. 2244, 2266 (2024).
[91] White House. (April 2025). Presidential Actions, Directing the Repeal of Unlawful Regulations. Available at: https://www.whitehouse.gov/presidential-actions/2025/04/directing-the-repeal-of-unlawful-regulations/

best meaning. PhRMA urges CMS to withdraw the "Bona Fide" qualifier because it is inconsistent with the single, best meaning of the statute.

The ordinary meaning of "marketing," which is also the way "marketing" is used in the pharmaceutical sector specifically, does not support CMS' narrowly-focused approach that departs from the best meaning of the relevant statutory text. For example, Merriam-Webster's dictionary defines marketing as "to expose for sale in a market."[92] In a Supreme Court case interpreting the meaning of "marketing" when the term was undefined in a statute, the Court looked to the "ordinary meaning" of the term and concluded that "[m]arketing ordinarily refers to the act of holding forth property for sale, together with the activities preparatory thereto.… The word does not require that the promotional or merchandising activities connected with the selling be extensive."[93] Thus, when "marketing" is undefined, the Court simply requires the product to be "for sale."[94] Whether a product is marketed should therefore be determined based on an objective standard, not on subjective assessments regarding the degree, scale, or commercial success of marketing activities.

These definitions also reflect the generally accepted, ordinary meaning of "marketed" in the context of a pharmaceutical product, and, consequently, the meaning of "marketed" that Congress intended in the context of the IRA. For instance, the ordinary meaning of "marketing" is consistent with FDA's conception of marketing under section 505(j) of the FDCA, which is relevant given that the IRA's QSSD and selected drug definitions reference a generic drug *"*marketed under section 505(j)."[95] In the context of 180-day exclusivity for first generic applicants, the FDCA provides that FDA shall not make effective a subsequent generic application until "180 days after the date of the first commercial marketing of the drug . . . by any first applicant."[96] In regulations, FDA defines the term "commercial marketing" (a term that is narrower than "marketing") as "the introduction or delivery for introduction into interstate commerce of a drug product described in an ANDA, outside the control of the ANDA applicant, except . . . for investigational use . . . or transfer of the drug product to parties identified in the ANDA for reasons other than sale."[97] Similarly, for purposes of implementing section 506I of the FDCA concerning required notifications to FDA about the marketing status of a product,[98] FDA considers a product's marketing status to depend on whether a product is distributed by the application holder, i.e., whether the product is available for sale.[99]

In contrast, the Proposed Rule imposes an extra-statutory limitation on what qualifies as marketing of a generic or biosimilar biological product for purposes of the QSSD definition and for determining whether

[92] Merriam-Webster.com. "Market." Available at: https://www.merriam-webster.com/

[93] *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 187 (1995)

[94] *Ibid.* ("One can market apples by simply displaying them on a cart with a price tag; or market a stock by simply listing it on a stock exchange; or market a house (we would normally say 'place it on the market') by simply setting a 'for sale' sign on the front lawn. Indeed, some dictionaries give as one meaning of 'market' simply 'to sell. ' See, *e.g.,* Oxford Universal Dictionary 1208 (3d ed. 1955); Webster's New International Dictionary 1504 (2d ed. 1950).").

[95] SSA § 1192(e)(1)(A)(iii); *see also id.* SSA § 1192(c)(1)(A)(i).

[96] FDCA § 505(j)(5)(B)(iv)(I).

[97] 21 C.F.R. § 314.3.

[98] Section 506I requires NDA and ANDA holders to provide written notification prior to withdrawing an approved product from sale and if the drug will not be available for sale within 180 days of the date of approval.

[99] FDA. (August 2020). Guidance for Industry: Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format. Available at: https://www.fda.gov/media/120095/download

a product ceases to be a selected drug or otherwise is no longer subject to the price setting process or to an MFP.

In this Proposed Rule, CMS has provided three examples to illustrate its analysis of "Bona Fide Marketing:"

1. If a potential QSSD has at least one approved generic drug or licensed biosimilar with "high and consistent PDE utilization, AMP sales, and/or ASP sales," CMS would consider that generic drug or biosimilar to be subject to Bona Fide Marketing.[100]

2. If a potential QSSD might "have a newly or recently approved generic drug or licensed biosimilar and the product has relatively low PDE utilization, AMP sales, and/or ASP sales,"[101] CMS explains that where it finds "in additional review of public information that the generic drug or biosimilar manufacturer has successfully launched their product, and there is no evidence of agreements limiting distribution of the generic drug or biosimilar," then CMS "may consider the generic drug or biosimilar of the potential [QSSD] to be subject to Bona Fide Marketing."[102]

3. If a potential QSSD might have an approved generic or licensed biosimilar product "with no PDE utilization, AMP sales, and/or ASP sales," if CMS finds "in additional review of public information that there are ongoing patent disputes and no generic drug or biosimilar manufacturer has successfully launched their product," then CMS "may consider the generic drug or biosimilar of the potential [QSSD] as not subject to Bona Fide Marketing."[103]

These examples largely mirror those included in the IPAY 2028 Final Guidance. However, CMS has modified the second example in a significant respect. The IPAY 2028 Final Guidance indicated that where "a potential [QSSD] might have a newly or recently approved generic or licensed biosimilar and the product has relatively low PDE utilization, AMP sales, and/or ASP sales," CMS "*will* consider the generic or biosimilar product of the potential [QSSD] as bona fide marketed."[104] The Proposed Rule now states only that CMS "may" reach that conclusion. This change introduces additional uncertainty into an already vague and unlawful standard. Moreover, the examples do not cure the statutory deficiencies of the "Bona Fide" qualifier. In addition, the third example should be deleted, as it would result in a determination that the generic drug or biosimilar is not "marketed" even where it is. For instance, this example would result in the wrong outcome where a particular biosimilar has recently launched, e.g., at risk or based on a settlement without any patent litigation proceedings as to its biosimilar (notwithstanding the existence of other patent disputes as to biosimilars of the same reference product), but PDE, AMP, and ASP sales do not yet reflect the launch.

CMS' approach conflicts with other provisions of the IRA.

CMS' imposition of the "Bona Fide" qualifier conflicts with other provisions of the IRA addressing the biosimilar "pause" and the treatment of authorized generics. Although Congress made no reference to "Bona Fide" marketing or any similar gloss in the QSSD or selected drug definitions, in other provisions

[100] 91 Fed. Reg. at 36,266.
[101] *Id.*
[102] *Id.*
[103] *Id.*
[104] IPAY 2028 Final Guidance at 170.

of the same section of the statute, CMS' proposed rule would expressly impose limitations on what qualifies as marketing. When "Congress includes particular language in one section of a statute but omits it in another section of the same Act," it is "generally presumed that Congress acts intentionally and purposely in the disparate inclusion or exclusion."[105] Congress's decision not to qualify the term "marketed" in the QSSD or selected drug definitions demonstrates that CMS' additional "Bona Fide" limitation conflicts with the statute. The same conclusion is reinforced by Congress's treatment of authorized generic drugs. In section 1192(e)(2), Congress specifically addressed products that are "marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging . . ., product code, labeler code, trade name, or trade mark than the reference product." This definition demonstrates that Congress knew how to impose additional commercialization-related conditions and distinctions when it deemed them relevant. Yet Congress did not require "bona fide" marketing in the QSSD definition, the selected-drug provisions, or the biosimilar-pause provisions. CMS therefore may not read an extra-statutory "bona fide" requirement into the term "marketed."

The IRA expressly prohibits manufacturers from receiving the biosimilars-based selection "pause" based on volume-limited arrangements. Specifically, section 1192(f)(2)(D)(iv) states that "[i]n no case shall the Secretary delay the inclusion of a biological product as a selected drug" if "the manufacturer of the biosimilar . . . entered into any agreement . . . with the manufacturer of the reference product . . . that . . . *restricts the quantity (either directly or indirectly)* of the biosimilar biological product that may be sold in the United States over a specified period of time."[106] Volume-limited arrangements were also known in the industry at the time Congress enacted the IRA. Clearly, then, Congress knew how to impose volume-based requirements or limitations and did so in the very same section of the statute but elected not to do so in the definitions of QSSD and selected drug.

The statute does not permit CMS to continually evaluate "Bona Fide Marketing".

Furthermore, there is no statutory mechanism that permits CMS to "monitor that the approved generic drug or licensed biosimilar continues to be subject to Bona Fide Marketing,"[107] *after* it determines that a potential QSSD will not be considered a QSSD or that a selected drug should be removed from the Program. Nonetheless, CMS states that it "will consider whether meaningful competition exists on an *ongoing basis* between any dosage form or strength of a potential qualifying single source drug that includes the listed drug or reference product and any one or more generic drug(s) or biosimilar(s)."[108] CMS seems to imply that it can *revisit* such determinations and potentially restore a product to "selected drug" status, even though this is not contemplated by the statute. The statute is clear that once a product is determined not to meet the definition of a QSSD or ceases to be a selected drug, it is no longer eligible for price setting. Instead, the statute provides explicitly that once a selected drug ceases to be a selected drug, CMS' agreement with the manufacturer "*shall no longer be effective*" and the drug "is no longer considered a selected drug."[109]

There is no statutory basis for CMS to restore selected drug status to a product that is no longer a selected drug or to enter into a new section 1193 agreement with a manufacturer after the parties' section 1193

[105] *Russello v. United States,* 464 U.S. 16, 23 (1983) (citations omitted).
[106] SSA § 1192(f)(2)(D)(iv) (emphasis added).
[107] 91 Fed. Reg. at 36,264 (emphasis added); Proposed 42 C.F.R. § 429.130(a).
[108] 91 Fed. Reg. at 36,264.
[109] SSA § 1193(b) (emphasis added).

agreement has terminated due to the approval and marketing of a generic or biosimilar. Further, the product's MFP and the manufacturer's agreement to provide access to that MFP to entities that dispense or administer the drug to Medicare beneficiaries are set forth in the agreement—which would have terminated. Accordingly, a whole new process of price setting procedures and setting an MFP for the drug would be needed for the Program to apply, but the statute never mentions or even hints at this extended series of events or any of its parts. Indeed, CMS' approach would effectively rewrite the scope of the IRA by permitting the Program to once again apply to products that Congress specifically removed from the Program following generic or biosimilar entry. Congress would not have authorized this approach of CMS ending a product's selected drug status, terminating the CMS-manufacturer agreement and then reinstating the drug's selected drug status and requiring the manufacturer to enter into a new agreement, without saying so expressly. Nor would Congress have silently delegated to CMS the unilateral authority to develop and carry out this far-fetched re-selected drug process. The absence of any statutory framework confirms that Congress did not intend to confer such authority. The statute provides no standards governing when CMS may "restore" selected-drug status after it has ended. Instead, CMS appears to claim open-ended discretion to determine if and when a product should be returned to the Program. Had Congress intended to create such a reinstatement regime, it would have specified the circumstances under which reinstatement is required or permitted and the procedures governing that process. CMS' approach has no statutory foundation and conflicts with the statute's express terms. It also would impermissibly expand CMS' authority beyond the limits established by Congress. Moreover, to the extent CMS is suggesting it has jurisdiction to police competition, and the expertise necessary to do so, that suggestion is incorrect. Instead, that authority rests with the agencies charged with enforcement of the antitrust laws.

IV. Orphan Drug Exclusion from QSSDs (§ 429.125(e)(1))

We provide two comments on the Proposed Rule's provisions on the orphan drug exclusion. First, CMS should finalize that it will apply the exclusion based on a drug's status as of the otherwise applicable selection date. Second, CMS should apply the orphan drug exclusion at the level of the individual drug or biological product approved under a single NDA or BLA, rather than across all products sharing an active moiety or active ingredient. Addressing both issues is necessary to ensure that the exclusion is administered consistent with the statutory text and Congress's intent to preserve incentives for orphan drug development.

CMS must apply the orphan drug exclusion based on a drug or biological product's status at the time of the otherwise applicable selection date.

CMS correctly recognizes that it must apply the orphan drug exclusion based on a drug's status at the time of the otherwise applicable selection date. In its discussion of the exclusion itself, CMS states that "[w]e would not consider withdrawn orphan drug designations or withdrawn approvals when determining whether a drug meets the orphan drug exclusion."[110] This approach is reflected in proposed 42 C.F.R. § 429.125(e)(1)(i)(B) and § 429.125(e)(1)(ii)(B) and indicates that CMS will consider a drug's eligibility for the orphan drug exclusion based on designations and approvals in place on the otherwise applicable

[110] 91 Fed. Reg. at 36,368; *see also id.* ("For purposes of the Negotiation Program, we use the term 'withdrawn' with respect to an orphan drug designation to refer to a voluntary withdrawal of an orphan drug designation as described at 23 CFR 316.24 or a revoked orphan drug designation as described at 23 CFR 316.29.").

selection date.[111] Section 1192(e)(3)(A) is written in the present tense and it exempts a drug that "is" designated for one or more rare diseases or conditions and "is" approved only for indications within such designated rare disease or condition. If those criteria are met on the otherwise applicable selection date, the drug is not a QSSD, and CMS lacks authority to treat it as one. CMS therefore should finalize its proposal and continue to apply the orphan drug exclusion based on the drug's status at the time of the otherwise applicable selection date.

This interpretation is also consistent with CMS' prior guidance. In the IPAY 2028 Final Guidance, CMS explained that it "will consider only active designations and active approvals when evaluating a drug for the Orphan Drug Exclusion" and "will not consider withdrawn orphan drug designations or withdrawn approvals when determining whether a drug meets the Orphan Drug Exclusion."[112] That guidance reflects an understanding that eligibility for the orphan drug exclusion depends on the drug's *current* orphan designation and approval status when CMS evaluates whether the exclusion applies in relation to a particular selection date.

In the separate discussion of the age requirement for former orphan drugs, CMS states that a drug ceases to qualify for orphan status on the date it is approved for a non-orphan indication, "irrespective of whether approval of such indication is later withdrawn."[113] CMS' proposed principle is appropriately limited to calculating the age of a former orphan drug under section 1192(e)(4).

The single, best reading of the statute is that the age-calculation rule of section 1192(e)(4) comes into play if the drug is otherwise eligible for selection, i.e., the orphan drug exclusion does not apply to the drug on the otherwise applicable selection date because it is then approved for a non-rare disease or condition or no longer subject to orphan drug designation due to withdrawal of an orphan designation. A drug that, at the time of the otherwise applicable selection date, satisfies the criteria in section 1192(e)(3) is excluded from the definition of a QSSD and therefore cannot be selected.

Consistent with this interpretation, if a drug ceases to qualify for the orphan drug exclusion because it is approved for a non-orphan indication but later again satisfies all of the criteria in section 1192(e)(3) because the non-orphan indication is withdrawn and only orphan-designated indications remain approved, the drug should once again qualify for the orphan drug exclusion. CMS should clarify that periods during which the drug qualifies for the orphan drug exclusion do not count toward the applicable seven- or eleven-year period under section 1192(e)(4), because the drug is excluded from the Program during those periods and therefore is not accruing time as a former orphan drug eligible for selection. Any contrary interpretation would be at odds with the statute and Congressional intent.

In summary, in the final rule, CMS should finalize its proposal that a drug meeting the criteria of section 1192(e)(3) on the otherwise applicable selection date is excluded from the definition of a QSSD and therefore may not be selected, regardless of whether the drug at some earlier point did not qualify because, for example, it had a non-orphan indication that was subsequently withdrawn. CMS should also make clear that its statement regarding non-orphan indications as part of the age-calculation rule "irrespective of whether approval of such indication is later withdrawn" is relevant only to determining

[111] 91 Fed. Reg. at 36,347.
[112] IPAY 2028 Final Guidance a 171.
[113] 91 Fed. Reg. at 36,262.

the applicable seven- or 11-year period for a drug that no longer qualifies for the orphan drug exclusion on the otherwise applicable selection date.

The orphan drug exclusion should be applied to the drug or biological products approved in a single NDA/BLA.

PhRMA maintains that CMS should determine the applicability of the orphan drug exclusion based on the specific drug or biological products approved in a single NDA or BLA, consistent with our proposed interpretation of the QSSD definition described above. Under the Proposed Rule, "[a] potential [QSSD] qualifies for the orphan drug exclusion if, for *all* dosage forms and strengths of such potential [QSSD]" the applicable criteria are met.[114] This interpretation indicates that CMS will aggregate multiple drug or biological products based on their active moiety or active ingredient and then subsequently evaluate each aggregated grouping to determine whether it meets the conditions of the orphan drug exclusion. Further, if any single drug product or biological product loses the exclusion, other products with the same active moiety or active ingredient and the same NDA/BLA holder would also lose the exclusion regardless of their individual orphan drug status. This interpretation of the orphan drug exclusion criteria extends the problems with the QSSD definition, potentially penalizing drugs that have successfully met the requirements for the orphan drug exclusion.

The shared active moiety and ingredient approach suffers from the same inherent flaws as CMS' proposed definition of a QSSD.

PhRMA believes a QSSD must be strictly limited to those drug or biological products approved by FDA in a single NDA or BLA. Since the orphan drug exclusion is explicitly defined as an exception from the definition of a QSSD, it logically follows that it should be applied on an NDA/BLA basis as well. Furthermore, each drug or biological product approved under an individual NDA or BLA must independently meet the age requirement, which should be calculated from the date the exclusion is lost, as discussed above.

In addition to aligning with the statute, this approach better preserves incentives for orphan drug research and development. Under CMS' interpretation, once the orphan drug exclusion is lost for a single drug product or biological product (e.g., due to its approval for a non-rare disease), there would be severely diminished incentives to pursue new orphan drug approvals for the same active moiety or active ingredient. This would have a chilling effect on the development of new therapies for rare diseases, as manufacturers would be discouraged from investing in additional orphan indications once the exclusion is lost for any product of theirs sharing the same active moiety or ingredient, regardless of the NDA or BLA. By adopting a NDA/BLA-specific approach, CMS can ensure that the incentives for orphan drug development remain robust, encouraging manufacturers to continue pursuing new treatments for rare diseases even if the exclusion is lost for a particular product.

V. Interpretation of Section 1192(c)(1) Regarding Timing of Generic or Biosimilar Entry (§ 429.135; § 429.130)

PhRMA disagrees with CMS' interpretation of section 1192(c)(1), as reflected in proposed §§ 429.135 and 429.130, that a selected drug remains subject to an MFP for an IPAY unless CMS determines that a

[114] Proposed 42 C.F.R. § 429.125(e)(1).

generic drug or biosimilar is approved or licensed and subject to Bona Fide Marketing by November 1 of the year that begins two years prior to the IPAY.[115] So long as CMS makes a determination of generic or biosimilar approval and marketing at least nine months prior to the relevant IPAY, the selected drug should not be subject to an MFP for that IPAY.

Consider a drug selected in February 2027 for IPAY 2029 for which CMS determines on March 1, 2028, that a generic drug has been approved and marketed. Section 1192(c)(1) states that "each negotiation-eligible drug included on the list published . . . *with respect to an initial price applicability year* . . . shall be *referred to* as a 'selected drug' with respect to *such year* and *each subsequent year* beginning before the first year that begins at least 9 months after the date on which the Secretary determines at least one drug or biological product" has been approved or licensed and marketed pursuant to such approval or licensure.

The provision should be read such that if the generic or biosimilar launches by March 31, 2028, the drug would no longer be "referred to" as a selected drug with respect to the year beginning on January 1, 2029, either because "such year" begins at least nine months after CMS' determination of generic approval and marketing; or because such year is a subsequent year that begins at least nine months after CMS' determination. Accordingly, the MFP would not go into effect in IPAY 2029. Before CMS made its determination of generic approval and marketing, the drug was "referred to as a 'selected drug' with respect [to IPAY 2029]"—consistent with the statutory language—as the manufacturer was required to submit data to CMS, engage in the price setting process, sign an MFP agreement, and have its MFP published.

The above approach helps promote competition by incentivizing market entry of generics and biosimilars, while also giving CMS a nine-month lead time to terminate selection of a branded drug after generic or biosimilar entry. By contrast, if CMS continues with its proposed interpretation, a generic or biosimilar launched more than a year before the IPAY begins (e.g., on November 2, 2027) would still have to compete against a price-set brand name drug beginning on January 1, 2029. PhRMA's position applies equally to future IPAYs as well.

[115] 91 Fed. Reg. at 36,265.

Appendix B: Negotiation Program Agreement (Subpart C)

CMS' proposals regarding the Negotiation Program Agreement significantly exceed the Agency's statutory authority in at least two important ways. The proposed concept and definition of "Primary Manufacturer" has no support in the statute and would impose wholly unauthorized obligations and burdens on entities that CMS deems to be "Primary Manufacturers." Second, CMS' proposal on CMS "review and approval" of novations when a Primary Manufacturer transfers a selected drug and the associated Negotiation Program Agreement lacks clarity and exceeds Agency authority.

I. Entrance into an Agreement with CMS (§ 429.200; § 429.20)

PhRMA continues to object to the "Primary Manufacturer" construct that CMS proposes to establish in section 429.20 and subpart C of part 429, including the requirement that the "Primary Manufacturer" enter into the Negotiation Program Agreement with CMS under 429.200. There is no support in the statute for a hierarchy among manufacturers whereby a Primary Manufacturer would be held accountable for the actions of other, Secondary Manufacturers. Rather, the statute defines "Manufacturer" as "any entity" engaged in a range of production or distribution-chain activities for prescription medicines.[116]

It is significant that this definition incorporates a chain of citations. Specifically, section 1191(c)(1) of the SSA states that the term, "manufacturer," has the meaning given that term in the Part B statute, at section 1847A(c)(6)(A). Section 1847A(c)(6)(A), in turn, defines manufacturer "as defined in section 1927" (i.e., the Medicaid drug rebate statute), but specifically authorizes the Secretary to exclude repackagers. Finally, section 1927(k)(5) of the Act defines manufacturer as "any entity" that engages in a wide variety of activities related to a prescription medicine, including packaging, repackaging, labeling, relabeling and distribution a prescription drug product (but excluding wholesalers and pharmacies under state law):

> The term "manufacturer" means any entity which is engaged in-
>
> > (A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or
> >
> > (B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.
> >
> > Such term does not include a wholesale distributor of drugs or a retail pharmacy licensed under State law.[117]

The IRA certainly does not indicate a clear Congressional intent to upend decades of corporate law that one corporate entity shall not be vicariously liable or responsible for the activities of another.[118] Yet,

[116] Section 1191(c)(1) of the Social Security Act (SSA) defines "manufacturer" with reference to the definition of that term in section 1847A(c)(6)(A) which in turn refers to the definition in section 1927(k)(5).
[117] SSA § 1927(k)(5).
[118] Fundamental corporate law principles provide that independent corporations are distinct legal entities with limited liability. See, e.g., Fletcher, Fletcher Cyclopedia of the Law of Corporations, §§ 28-29; Phillip I. Blumberg, Limited Liability and Corporate Groups, 11 J. Corp. L. 573, 591–592 (1986); Franklin A. Gevurtz, The Globalization of Corporate Law: The End of

under CMS' reading, although CMS recognizes the Secondary Manufacturer is an entity separate from the Primary Manufacturer, it still expects the Primary Manufacturer to enter into an agreement whereby it "negotiates" on behalf of the separate entity, agrees that the separate entity will provide access to the MFP, and agrees that it will submit information held by the separate corporate entity all under the threat of crippling penalties that would be imposed only on the Primary Manufacturer.

In the preamble, CMS points to section 1193(a)(1), which CMS characterizes as "establish[ing] that CMS will negotiate, or renegotiate, as applicable, an MFP with '***the*** manufacturer' of the selected drug."[119] However, section 1193 starts off with a general statement that the Secretary shall "enter into agreements with manufacturers of selected drugs."[120] Only after this preface does the statute refer to "the" manufacturer. Use of the article "the" in this context is simply acknowledging that each distinct manufacturer will have a distinct agreement, and "the" manufacturer signing such individual agreement is subject to certain statutory requirements. In other words, "the" in this context is not specifying that there can be only one manufacturer *per QSSD*. Instead, it is specifying that there should be one manufacturer *per agreement*, but there may be many different agreements, even for the same QSSD, as CMS has defined that term.

PhRMA urges CMS to take the opportunity presented by this initial notice-and-comment rulemaking that will establish policies and requirements for the future of the Program to reconsider this proposal altogether. Barring that, PhRMA requests that CMS establish policies to address the significant legal and operational problems it creates.

If CMS intends to finalize the policy as proposed, the Agency should adopt protections to ensure that Primary Manufacturers are not unfairly held accountable for the actions or noncompliance of third parties outside their control. For example:

- Safe harbors for Primary Manufacturers that engage in good-faith efforts to obtain information and ensure Agreement compliance; and
- Notice of violation and a reasonable opportunity to cure any Program violation by a Secondary Manufacturer or other entity prior to any enforcement action.

II. Other Provisions of the Negotiation Program Agreement (§ 429.210)

In 429.210(c), CMS proposes to codify its current guidance that when a Primary Manufacturer of a selected drug transfers ownership of one or more NDAs or BLAs, as applicable of a selected drug, the Primary Manufacturer remains responsible for all requirements of the 1193 agreement unless the new entity assumes responsibility for the agreement.

PhRMA notes that CMS has never explained why it would not allow a Primary Manufacturer to transfer only a portion of an agreement when only some of the NDAs or BLAs that might make up the qualifying single source drug are being transferred. CMS' extra-statutory definition of QSSD creates a scenario where CMS can interfere with marketplace decision-making in cases where an entity wishes to transfer

History or A Never-Ending Story? 86 Wash. L. Rev. 475, 487 (2011); Douglas G. Smith, A Federalism-Based Rationale for Limited Liability, 60 Ala. L. Rev. 649, 667 (2009). We also refer CMS to our previous comments, particularly on section 40 of the IPAY 2026 Initial Guidance.

[119] 91 Fed. Reg. at 36267 (emphasis added).

[120] *See also* SSA § 1191(a)(2).

only some NDAs/BLAs that comprise the QSSD. Indeed, by insisting that the Primary Manufacturer must remain responsible for all or none of the QSSD, CMS inserts itself into corporate decision-making. This is not within the remit of CMS – and CMS should revise its policy to allow novation of only some NDAs/BLAs in cases where a QSSD includes more than one NDA/BLA.

In the Proposed Rule, CMS proposes to add a new requirement that CMS must "approve and sign" any novation allowing the acquiring entity to become the successor in interest to the transferring Primary Manufacturer. CMS proposes no standards or time frame for such approval and signature.

First, CMS lacks authority for the proposal. An entity that no longer owns the product is not "manufacturing" the drug." The 1193 agreement is best read not as a negotiated contract – but merely a reflection of an "opt-in agreement that memorializes the statute and regulations."[121] Thus, CMS must have clear statutory authority to impose liability on entities no longer manufacturing drug products. That authority does not exist. Even CMS' own definition of "Primary Manufacturer" in proposed § 429.20 recognizes that if the entity is not the NDA holder or BLA holder, it is not the "manufacturer."

CMS cites to section 1193(a)(5) of the Act to argue that "the manufacturer must comply with requirements determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program." But it is not "necessary" to require a manufacturer to comply with vague standards – with no regulatory deadline – and for CMS to maintain unmitigated authority to interfere with commercially viable sales. "Necessary" means "absolutely needed"; "required."[122] CMS does not explain why all parts of its novation policy are absolutely needed to administer and monitor the MDPNP.

Second, even if the novation and signature/approval requirements were authorized, the agency acts arbitrarily and violates notice-and-comment rulemaking by not providing any explanation of the standards for approving (or not approving) a novation. Nor does CMS propose any deadline for when it will act, or what recourse a manufacturer has if CMS fails to act on the novation. At the very least, CMS must subject to comment (in a new proposed rule) proposed standards for when CMS may or may not approve a novation. CMS should also propose a time frame, create a process for a manufacturer to challenge excessive time delays, or deem the novation approved if CMS has not acted within 30 days of submission.

[121] 83 Fed. Reg. 12770, 12771 (Mar. 23, 2018).
[122] Merriam-Webster.com. "Necessary." Available at: https://www.merriam-webster.com/dictionary/necessary.

Appendix C: Program Administration (Subpart D)

The recommendations below focus on protecting highly sensitive manufacturer information and ensuring strong confidentiality, cybersecurity and data governance safeguards.

Key Recommendations:

- Develop robust confidentiality and security implementation protocols, including the solicitation and incorporation of feedback from manufacturers;
- Protect confidential information to the full extent provided under section 1193(c), develop and share confidentiality and security implementation protocols for comment, and ensure contractors and others with access to manufacturer data have agreements that adequately protect proprietary information;
- Treat non-public information relating to R&D, including but not limited to FDA applications and approvals, as categorically proprietary.

I. Confidentiality Policy and Data Use (§ 429.300)

PhRMA appreciates CMS' repeated recognition that a large proportion of the data submitted by manufacturers is highly sensitive and proprietary. As noted in our previous comments, section 1193(c) of the SSA specifies Congress' intent to protect from public release any confidential information provided by manufacturers to HHS in the context of the price setting program. The statute provides the following:

> (c) CONFIDENTIALITY OF INFORMATION.—Information submitted to the Secretary under this part by a manufacturer of a selected drug that is proprietary information of such manufacturer (as determined by the Secretary) shall be used only by the Secretary or disclosed to and used by the Comptroller General of the United States for purposes of carrying out this part.

PhRMA is unaware of any other program that would compile such a large volume of biopharmaceutical innovator information in one repository—on R&D costs, revenues, patents, production and distribution costs, market pricing and other highly sensitive and proprietary data. Congress was clearly aware of the sensitivity of data to be collected, as it included in the IRA an unusually restrictive limitation, applying not just to disclosure of manufacturer-submitted data but also their "use." Only the Secretary (or Comptroller General in certain situations) may use the data, and then, only to carry out the price setting Program.[123]

We support CMS' codification of the principle in the proposed regulation that the vast amounts of proprietary information submitted should be exempt from the Freedom of Information Act (FOIA) disclosures under Exemptions 3 and/or 4, as proposed paragraph 429.300(b).[124] PhRMA also continues to recommend manufacturers have the opportunity to designate their own information as proprietary or

[123] SSA § 1193(c).
[124] United States Department of Justice. What are the 9 FOIA Exemptions? Available at: https://www.justice.gov/d9/what_are_the_9_foia_exemptions.pdf. We also note that CMS proposes in § 429.300(b) to evaluate whether information "meets the requirements set forth under Exemption 3 or Exemption 4" of FOIA. However, in the event FOIA standards for protecting confidential, commercial information are less protective than the IRA, the IRA requirements in section 1193(c) would of course prevail. Moreover, the information deemed proprietary, as set forth in § 429.300(c) should not be released (or used by any person other than those listed in 1193(c) and for any purpose other than price setting) unless already publicly available, without the need for an additional layer of analysis under FOIA.

confidential, requiring CMS to prove why the information should be made publicly available prior to any disclosure, and that such a rule be codified in CMS regulations.

PhRMA further strongly encourages CMS to affirm that nothing in the guidance shall override the full range of other potentially applicable privacy and confidentiality laws. In addition to FOIA, the Trade Secrets Act is a criminal statute that prohibits government disclosure of information that "concerns or relates to the trade secrets, processes, operations, style of work, or apparatus, or to the identity, confidential statistical data, amount or source of any income, profits, losses or expenditures of any person, firm, partnership, corporation, or association."

Confidentiality and Security Protection Protocols

PhRMA also notes that confidentiality and data security are complex topics, and a regulation with clear, strong prohibitions on disclosure and unauthorized use of the types of proprietary data manufacturers submit to CMS under this program is critical but not sufficient in this context. ***CMS must, after finalizing its regulations, develop robust confidentiality and security implementation protocols to implement the regulation, including the solicitation and incorporation of feedback from manufacturers to ensure protection of the Agency's unprecedented and vast collection of proprietary information from manufacturers.***

At a minimum, any confidentiality policy must require:

- Access to any information received is limited to the smallest number of employees and other personnel possible, as well as the minimum data necessary, and such personnel are inventoried and recorded on a regular basis (including an explanation of such individual's legitimate need to use the information and purpose);
- Execution of non-disclosure agreements by any individuals with access to the data (including contractors and staff) as a pre-condition to access, under which they are restricted from improperly using or disclosing any proprietary information received during their employment/engagement and in perpetuity post-employment;
- Destruction of data by any individuals with access to the data when any Agreement terminates. CMS, the Comptroller General, or any part of the U.S. Department of Health and Human Services (HHS) that accesses information maintains policies as to how and when it will destroy proprietary information of the manufacturer, informs the manufacturer of such destruction and documents compliance with destruction policies;
- Notification to any submitters of any erroneous use or disclosure of proprietary information, even if inadvertent, and how it intends to remedy such use or disclosure;
- Notification to manufacturers any time data are shared outside of CMS (for example with a contractor) or CMS intends to use such data for purposes unrelated to price setting (for example, because CMS determines the data are not proprietary), the rationale for such sharing/use, and providing manufacturers with a robust prior opportunity to object to such sharing/use, along with an adjudication process. If CMS determines that otherwise proprietary information is nevertheless "publicly available," CMS should explain such reasoning prior to allowing such information to be used (and provide for a period of adjudication before the data could be shared or released). Again, such notification must

extend not just to public disclosure, but also any "use" or disclosure outside CMS, including to Congress or other agencies; and

- Referrals made to the Department of Justice regarding violations of criminal laws prohibiting the publication, divulging, disclosure, or making known in any manner or to any extent not authorized by law, trade secret or confidential commercial information.

The government has a history of requiring non-disclosure agreements from contractors and others under agreement, and PhRMA is happy to share templates.[125]

CMS should put forward a security policy as well, explaining how it will ensure the cybersecurity of systems holding manufacturer-specific data. The security protocol must include limited access to only certain personnel via secure portal; procedures on secure encrypted transmission mechanisms (as approved by HHS' Chief Information Officer and Office of the General Counsel); secure storage; inability to download confidential information to removable media or any other portable storage; policies on and tracking of any printing or screenshotting of confidential information (including watermarking of electronic and paper copies with a "confidential" label, safeguards that only a minimum amount may be printed, and standards that printouts remain within a particular physical location from which they cannot be removed, along with locked offices and file cabinets).

For the reasons stated above, ***PhRMA recommends that CMS protect confidential information to the full extent provided under section 1193(c) of the SSA consistent with FOIA and other applicable confidentiality and data privacy laws, develop and share its confidentiality and security implementation protocols for comment, and ensure contractors and others with access to manufacturer data have agreements with CMS that adequately protect the high volumes of proprietary information CMS collects.***

Designation of Additional Categories of Information as Proprietary Information

Beyond the general provisions defining confidential information, CMS proposes to designate specific categories of primary manufacturer data as proprietary information in paragraph 429.300(c). PhRMA appreciates and supports these designations, particularly non-FAMP price data.

At the same time, PhRMA suggests that the list proposed is under-inclusive. While CMS proposes to deem proprietary a Primary Manufacturer's research and development costs of the selected drug, it should also provide that information related to R&D, including but not limited to applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Services Act, be deemed proprietary. As a general matter, disclosure of R&D-related information to the public and competitors is extremely likely to result in harm to a manufacturer. As such, this information warrants rigorous protection. While PhRMA recognizes that regulatory approvals ultimately may be made public, information in pending marketing applications is typically proprietary and highly sensitive and is protected from disclosure by federal law. This sensitivity remains after approval, with much data and information in approved applications remaining protected confidential commercial

[125] Clauses CMS should add to any contracts or other Agreements include HHS Acquisition Regulations 352.224-71, and clauses similar to H3 and H.6, respectively, available at: "Confidential Information"; and https://www.hhs.gov/sites/default/files/gram-contract.pdf (H.3, the "Disclosure of Information" clause, is at page 22 of this document and clause H.6 is at pages 23-24). *See also* https://www.hhs.gov/sites/default/files/vaccine-agreement-with-glaxo-smith-kline-modifications-1-and-2.pdf.

information and trade secrets exempt from disclosure. Under the Food and Drug Administration's (FDA) regulations, the existence and status of a pending application, in addition to information contained in a pending NDA or BLA, generally are protected from public disclosure.[126] The FDA adopted this regulation to implement the Federal Trade Secrets Act, FOIA, and section 301(j) of the FD&C Act, which all protect such information from public disclosure, and has long regarded this information as competitively sensitive for which disclosure would cause competitive harm.[127] Only once a decision on an application is final will certain information regarding the application be subject to potential disclosure, and even then, other information within the application remains protected.[128]

Consistent with FDA protection from disclosure of information about and within pending marketing applications, PhRMA recommends that CMS revise paragraph 429.300(c) to provide that CMS will treat non-public information relating to R&D, including but not limited to FDA applications and approvals, as categorically proprietary.

[126] See 21 C.F.R. §§ 314.430(b) ("FDA will not publicly disclose the existence of an application … before an approval letter … or tentative approval letter is sent to the applicant …, unless the existence of the application … has been previously publicly disclosed or acknowledged."); *Ibid* § 314.430(c) ("If the existence of an unapproved application or abbreviated application [for a small molecule drug] has not been publicly disclosed or acknowledged, no data or information in the application or abbreviated application is available for public disclosure."); *Ibid* § 601.51(b) ("The existence of a biological product file will not be disclosed by [FDA] before a biologics license application has been approved unless it has previously been publicly disclosed or acknowledged."), *Ibid* § 601.51(c) ("If the existence of a biological product file has not been publicly disclosed or acknowledged, no data or information in the biological product file is available for public disclosure."); see also 39 Fed. Reg. 44,602, 44,634 (Dec. 24, 1974) ("The existence of a pending NDA constitutes confidential commercial information where the existence of clinical testing has not previously been publicly disclosed or acknowledged.")

[127] 39 Fed. Reg. at 44,634.

[128] 21 C.F.R §§ 314.430(f), (g), 601.51(e), (f).

Appendix D: Establishment of Single MFP and Determination of Ceiling (Subpart E)

The recommendations below seek to ensure that CMS methodologies accurately reflect product value, accommodate variation across therapies, and apply statutory pricing provisions as written.

Key Recommendations:

- Add flexibility and work with Primary Manufacturers at the start of the negotiation process to align on the best analytical approach to calculating a single ceiling price and MFP for each selected drug, along with therapeutic alternatives;
- Explicitly recognize the need for a different approach for once-per-lifetime products and products administered infrequently;
- Utilize labeled dosing regimens as opposed to claims data (or at a minimum exclude outliers in calculations derived from claims data) and improve transparency in the calculations;
- Be flexible and work with Primary Manufacturers to agree on the best approach to the basis for calculating a single ceiling price and single MFP for each selected drug;
- Continue to assess feedback on an approach that adequately reflects expected costs of a medicine across the duration of treatment and therapeutic effect and whether, and how, one-time administration products should be compared against treatments with more traditional administration frequencies;
- Use FDA-approved dosage regimens to set 30-day equivalent supplies for Part B and Part D covered drugs;
- Engage with manufacturers and stakeholders about existing approaches to calculating 30-day equivalent supplies;
- Provide greater transparency into how the single MFP, therapeutic-alternative calculations, and starting point for price setting are determined;
- Modify the weighting in § 429.435(a)(4)(iv) to rely on the 30-day equivalent supply product mix rather than total-unit product mix;
- Revise proposed § 429.440(b)(4) so that when the ceiling is below the Temporary Floor, the ceiling limitation does not apply and the MFP may not be less than the Temporary Floor.

I. Calculation of the 30-Day Equivalent Supply (§ 429.415)

PhRMA continues to have numerous concerns with CMS' proposed approach to the calculation of a single ceiling price and MFP based on a 30-day equivalent supply if applied to all medicines covered under Part D and all medicines covered under Part B.[129] PhRMA appreciates that CMS' proposed methodology will be appropriate for many medications and supports the approach in those cases. As detailed below, however, the reliance on claims data to establish the 30-day equivalent supply can lead to undervaluing certain medicines and undervaluing appropriate adherence to medication regimens, particularly for medicines administered on a less frequent basis. Further, the 30-day equivalent supply approach presents particular challenges for medicines with one-time administration, an issue that CMS takes up in the Proposed Rule, underscoring the legitimacy of PhRMA's concerns with the current approach.

[129] Proposed 42 C.F.R. §§ 429.400(a)(1), 429.415.

The 30-day equivalent supply approach can also present challenges for medicines with variable dosing, for example with dosing that varies based on a patient's body weight or with dosing that varies based on the treatment phase of the condition.

Given this, PhRMA strongly recommends that CMS:

- ***Add flexibility and work with Primary Manufacturers at the start of the negotiation process*** to align on the best analytical approach to calculating a single ceiling price and MFP for each selected drug, along with therapeutic alternatives. For instance, for some products a per unit approach would lead to a more accurate calculation of a single ceiling price and MFP, and medicines where utilization varies widely patient-to-patient could benefit from drug-specific approaches.
- ***Explicitly recognize the need for a different approach for once-per-lifetime products and products administered infrequently***. CMS' proposal to calculate the 30-day equivalent supply for such products by assigning a value of 12 does not appropriately reflect the value of these products relative to other, more regularly dispensed or administered products.
- If CMS moves forward with codifying its current 30-day equivalent supply approach without added flexibility, we urge CMS to make a number of changes to its current methodology, including ***utilizing labeled dosing regimens as opposed to claims data (or at a minimum excluding outliers in calculations derived from claims data) and improving transparency in the calculations.***

We address each of these considerations, in turn.

Flexibility for Alternative Approaches Agreed to Between CMS and Manufacturers

As CMS has likely experienced in selecting and setting prices for IPAY 2026, 2027, and 2028 drugs, pricing and dispensing patterns for drugs can vary significantly by product. This variation means that adopting a single approach to calculating a single MFP and ceiling price for selected drugs can result in an outcome that is highly inaccurate for certain products and that can lead to undervaluing medicines. Because of this, PhRMA encourages CMS to recognize the need for flexibility to address specific circumstances and work with manufacturers to identify the best approach for a particular selected drug. For example, a per unit approach may work well for many drugs administered as oral tablets, whereas a per-unit approach may not be well-suited to Part B covered drugs reimbursed under multiple Healthcare Common Procedure Coding System (HCPCS) codes where pricing per unit varies across codes.

The 30-day equivalent supply approach can also present unique challenges for medicines with dosages that change based on body weight, indication, progression of treatment, or for other reasons. For example, patients with different body weights or different dietary patterns will require different amounts of insulin over a period of 30 days for the treatment of Type I diabetes. Patients with asthma will have highly variable utilization of rescue inhalers depending on how well controlled their condition is and environmental factors. And treatments for many autoimmune conditions require more frequent administrations early in the course of treatment, followed by less frequent administrations once a condition has been stabilized. CMS' proposed 30-day equivalent supply approach obscures these types of important differences in dosing and can lead to the undervaluing of these types of medicines.

Inconsistencies between calculations of the 30-day equivalent supply for therapeutic alternatives and selected drugs can result in an inappropriately low starting point for price setting. Because the starting point for a selected drug is solely based on the 30-day equivalent supply of its therapeutic alternatives, inconsistent methodologies can have significant implications for manufacturers of selected drugs. While the Proposed Rule would apply CMS' 30-day equivalent supply calculation approach to both selected drugs and therapeutic alternatives, PhRMA is concerned that the same approach is not being applied to therapeutic alternatives in practice. We strongly recommend that CMS be more transparent about its 30-day equivalent supply calculations for therapeutic alternatives going forward.

We urge CMS to be flexible and work with Primary Manufacturers to agree on the best approach to the basis for calculating a single ceiling price and single MFP for each selected drug starting with Part B and Part D covered drugs selected for IPAY 2029.

Such flexibility may be somewhat more complex to articulate through rulemaking, but CMS could detail in regulations a default approach for calculating a single ceiling price while also stipulating in regulation that a different approach may be used upon mutual agreement of CMS and the manufacturer. CMS itself recognizes the need to potentially vary the 30-day equivalent supply approach to "promote[] comparability"—proposed § 429.510(d)(2)(iv) would allow the Agency to depart from its method for calculating the 30-day equivalent supply to use a "tailored methodology that promotes comparability between the therapeutic alternative(s) and the selected drug." Having embraced the benefits of flexibility, CMS should expressly provide in regulations for alternative approaches in agreement with manufacturers to arrive at the best approach for selected drugs and therapeutic alternatives, and to appropriately carry out its section 1196(a)(2) responsibility to establish procedures for applying the MFP across different dosage forms and strengths.

Flexibility Around 30-Day Equivalent Supply for Single-Administration Drugs and Infrequently Administered

While CMS must establish an appropriate 30-day equivalent supply value for single-administration products, the Agency's proposed approach risks significantly undervaluing single-administration products relative to their therapeutic alternatives.

CMS' proposal to assign a fixed value of 12 as the 30-day equivalent supply for selected drugs that are "typically administered one time (for example, some vaccines, gene therapies, and cancer therapies)" treats such products effectively as if they provide only one year of therapeutic benefit for purposes of calculating the single MFP per 30-day equivalent supply, converting Part B data, and informing comparisons to therapeutic alternatives. [130] This wholly irrational approach risks systematically understating the duration and value of truly durable, one-time therapies.

We also urge CMS to consider that its current approach to calculating a 30-day equivalent supply results in a similar systematic understating of value for products that while not typically administered one time are instead administered once every few years (e.g., a tetanus, diphtheria and pertussis booster that is typically administered once every ten years). These types of products are also deserving of a unique approach for determining their 30-day equivalent supply.

[130] 91 Fed. Reg. 36,237; proposed § 429.415(a)(2).

Consider two examples:

- A cell therapy for cancer that has an expected treatment duration of at least 10 years. Medicare beneficiaries receiving this medicine would expect to be treated only once during their lives. Applying the Agency's "days between services" construct, the days between services would be calculated as 10 × 365 = 3,650 days between service, and the 30-day equivalent supply would be 3,650 / 30 = 121.67. But under the method CMS proposes, the Agency would assign a fixed default 30-day equivalent supply of 12.
- A meningococcal vaccine booster with expected administration every five years for individuals at ongoing increased risk (such as individuals with certain immunocompromising conditions). Under CMS' proposed "days between services" construct, the days between services would be calculated as 5 × 365 = 1,825 days between service, and the 30-day equivalent supply would be 1,825 / 30 = 60.8—significantly greater than the 30-day equivalent supply of 12 that CMS would assign for a one-time administration product and also likely higher than CMS would calculate utilizing the current "days between service" approach for Part B drugs that are not one-time products.

The use of a value of 12 rather than a larger number that would more accurately account for the years of therapeutic benefit from a one-time or infrequently administered medicine would significantly exaggerate the cost of these medicines in relation to therapeutic alternatives with more frequent or common dosing schedules. Moreover, that exaggerated cost directly affects CMS' calculation of its starting point for price setting based on the cost of therapeutic alternatives. For instance, consider the hypothetical one-time cell therapy discussed above and assume a price of $300,000. CMS may identify as a therapeutic alternative an infused oncology product administered once every 30 days with a price of $10,000 for each dose. Applying CMS' proposed 30-day equivalent supply value of 12 for the one-administration cell therapy, the cell therapy's price per 30-day equivalent supply would be calculated as approximately $25,000 ($300,000 ÷ 12), making it appear two and a half times more expensive than the monthly infused alternative.[131] But if CMS were to instead utilize the 121.67 30-day equivalent supply for the one-time cell therapy as calculated above, the cell therapy's price per 30-day equivalent supply would be $2,465.69, much lower than the infused oncology alternative.

Furthermore, the above cell therapy example reflects additional, indirect costs and value that are not adequately incorporated into the proposed methodology. Whereas the hypothetical cell therapy is administered once, the therapeutic alternative (i.e., an infused oncology product administered once every 30 days) requires a patient to undertake additional administrative and logistical burden to receive treatment. And in addition, the infused oncology product may not have a typical treatment duration that is confined to one year, further complicating the comparison of these products. Longer-acting therapies (e.g., long-acting injectables) demonstrate positive associations with medication adherence across diabetes, cardiovascular diseases, and mental health conditions like bipolar disorder and schizophrenia,

[131] The illustrative example above also helps to demonstrate why the Agency's proposed alternative approach for one-time administration products (to use a price-per-administration or price per HCPCS billing unit in lieu of a price per 30-DES, see 91 Fed. Reg. 36277) could even more significantly under-value these products in comparison to therapeutic alternatives, and as such, is even more problematic. The hypothetical one-time cell therapy would have a price-per-administration of $300,000 whereas the infused oncology therapeutic alternative would have a price-per administration of $10,000, making the one-time cell therapy 30 times more expensive than its competitor.

potentially improving overall health outcomes and, therefore, therapeutic benefit.[132] These benefits should be reflected in CMS' evaluation and is yet another reason why long-acting or once in a lifetime treatments should not be treated as effectively annual treatments.

Given the potential for the proposed methodology to significantly undervalue one-time administration products, ***PhRMA encourages CMS to continue to assess feedback from stakeholders on an approach that adequately reflects expected costs of a medicine across the duration of treatment and therapeutic effect and whether, and how, one-time administration products should be compared against treatments with more traditional administration frequencies***. CMS could consider adopting a meaningfully higher 30-day equivalent supply for single-administration products or a flexible methodology that more fully takes into account the real costs associated with each therapy. A flexible approach would also permit CMS to adopt a different 30-day equivalent supply calculation for products that, like the meningococcal example provided above, are not strictly single-administration but are administered with significant gaps in time between services. At a minimum, CMS must clearly delineate the scope of medicines to which the proposed fixed 30-day equivalent supply value of 12 would be assigned.

While CMS proposes in regulation a specific methodology for one-time administered products under Part B, it is also worth noting that single-administration products (and products that are administered with significant gaps between service) are not limited to those payable under Part B. Certain Part D covered products, including vaccines, can also be single-administration or infrequently administered. CMS should therefore modify its proposed approach in § 429.415(a) to make clear that it may employ a flexible or differentiated method for one-time or infrequently administered medicines covered under either Part B or Part D. In particular, for Part D covered vaccines that are expected to be administered once but are split over multiple doses in practice (e.g., an initial dose followed by a second dose two months later), CMS should consider proposing in rulemaking appropriate adjustments to ensure the 30-day equivalent supply accurately captures the intended course of therapy without undervaluing it. This is essential, as vaccines, whether administered once or infrequently as boosters over time, are significantly undervalued under CMS' current approach to 30-day equivalent supply calculations.

Modifications to CMS' Standard 30-Day Equivalent Supply Methodology

For selected Part B and Part D covered drugs where the Agency and Primary Manufacturer agree that a 30-day equivalent supply approach is more appropriate (or if CMS finalizes its proposal to use a 30-day equivalent supply approach across all selected drugs), we strongly recommend the following changes for both Part D and Part B covered drugs:

- ***CMS should use FDA-approved dosage regimens to set 30-day equivalent supplies for Part B and Part D covered drugs.*** If CMS does not use approved dosage regimens, then CMS should stipulate in regulation that the Agency's calculations of 30-day equivalent supplies do not exceed FDA-approved dosage regimens for selected drugs. We also urge CMS to exclude obvious outliers in calculating 30-day equivalent supplies using claims data. This would align with how the Medicare program excludes outliers in other types of program administration calculations.

[132] Rathore G., Singh R.P. (2025). Transforming disease management: The clinical benefits of long-acting injectable drug delivery systems. *Intelligent Hospital.* Available at: https://www.sciencedirect.com/science/article/pii/S3050837125000013.

- Prior to the start of the price setting process for a given selected drug, CMS should engage with the Primary Manufacturer and other stakeholders about existing approaches to calculating 30-day equivalent supplies. Manufacturers have significant experience with calculating 30-day equivalent supplies under certain state drug price transparency reporting requirements, and there are certain vendors that assist manufacturers with these calculations. PhRMA suggests that CMS speak with manufacturers and these vendors to better understand how 30-day equivalent supplies are calculated for medicines, particularly medicines falling into one of the more complicated situations described above, such as medicines with dosages that vary by indication or during the course of treatment. For example, for medicines with dosages that vary by the patient's weight, manufacturers today can calculate 30-day equivalent supplies by relying on the average weight of patients.
- CMS should provide greater transparency into how it calculates the single MFP for each selected drug, along with any of its therapeutic alternatives, and how it calculates the starting point for price setting. This is particularly the case if CMS utilizes different approaches for different selected drugs and their therapeutic alternatives. CMS should also report the estimated 30-day equivalent supply as part of the publicly released MFP files, along with the underlying calculation inputs to show how the MFP per package (and per HCPCS code for Part B covered drugs) was calculated.

II. Determination of the Applicable Average non-FAMP Amounts and Applicable Percent of the Average non-FAMP (§ 429.435)

While CMS describes the approach proposed in § 429.435(a)(4) to determine a single average non-FAMP ceiling price across all NDC-11s of a given drug as "consistent" with the methodology included in section 60.2.3 of the prior Guidance,[133] PhRMA notes that the calculation steps established in § 429.435(a)(4)(i) through § 429.435(a)(4)(viii) do not result in the same non-FAMP ceiling price for a given drug when compared against the steps established in sections 60.2.3(1) through 60.2.3(11) of the IPAY 2028 Final Guidance.

We urge CMS to modify the weighting in § 429.435(a)(4)(iv) to instead rely on the 30-day equivalent supply product mix as opposed to utilizing the product mix based on total units. This will address the discrepancy from prior guidance and ensure that calculations under § 429.435(a)(4) are consistent with those under 60.2.3.

As an illustrative example, consider the following **TABLE A** – a hypothetical short-monopoly selected drug covered under Part D:

TABLE A NDC-11	Description	PDE Units	PDE Unit Mix (%)	Avg Units per 30-day Equivalent Supply (30-DES)	Total 30-DES	30-DES Mix (%)
12345-0123-01	5mg 120ct	390,000	83.9%	60	6,500	71.8%
12345-0124-01	10mg 30ct	54,000	11.6%	30	1,800	19.9%

[133] 91 Fed. Reg. at 36290.

12345-0124-02	10mg 60ct	21,000	4.5%	28	750	8.3%
Total		**465,000**	**100.0%**		**9,050**	**100.0%**

The following steps calculate the average non-FAMP per 30-day equivalent supply across all three NDC-11s as established in section 60.2.3 of the IPAY 2028 Final Guidance. For ease, this illustrative example assumes that the non-FAMP values apply across the full calendar year, ignores growth at the Consumer Price Index for All Urban Consumers (CPI-U), and starts with assumed non-FAMP values per unit for each NDC-11 (Step 2):

Step 2: Non-FAMP per unit

The 5mg strength NDC-11 has an assumed non-FAMP per unit of $10.00, while the other two NDC-11s have assumed non-FAMPs of $20.00 per unit.

NDC-11	Non-FAMP per Unit
12345-0123-01	$10.00
12345-0124-01	$20.00
12345-0124-02	$20.00

Step 3 and Step 4: Calculate a non-FAMP per unit across the year

For ease, the example will assume the non-FAMP per unit values in the table above apply across the full year.

Step 5: Calculate the weighted non-FAMP per unit for each NDC-11 by NDC-9 PDE unit mix

In preparation for rolling-up the non-FAMP per unit to the NDC-9 level, calculate the non-FAMP per unit for each NDC-11 weighted by the PDE unit mix at the NDC-9 level. In other words, because the NDC-9 ending in "0124" is associated with two NDC-11s, the mix of each NDC-11 within the NDC-9 is calculated.

NDC-11	Non-FAMP per Unit [A]	PDE Unit Mix by NDC-9 (%) [B]	Weighted non-FAMP per Unit [A] x [B]
12345-0123-01	$10.00	100.0%	$10.00
12345-0124-01	$20.00	72.0%	$14.40
12345-0124-02	$20.00	28.0%	$5.60

Step 6: Roll-up the non-FAMP per unit by NDC-9

Sum up the weighted non-FAMP per unit to the NDC-9 level.

NDC-9	Weighted non-FAMP per Unit

12345-0123	$10.00
12345-0124	$20.00

Step 7: Grow calendar year 2021 calculation by CPI-U

For ease, the example will skip this step.

Step 8: Identify the applicable percent

Since this illustrative drug is a short-monopoly product, the applicable percent is 75%.

Step 9: Calculate the average non-FAMP ceiling per 30-day equivalent supply for each NDC-9

Multiply applicable percent from step 8 by the weighted non-FAMP per unit for each NDC-9. Divide this product by the quotient of the total PDE units divided by average units per 30-day equivalent supply. Multiply these values together to get the non-FAMP ceiling per 30-day equivalent supply.

NDC-9	Weighted non-FAMP per Unit [A]	Applicable % [B]	Non-FAMP Ceiling per Unit [A] x [B] = [C]	Total PDE Units / 30-DES [D]	Non-FAMP Ceiling per NDC-9 [C] x [D]
12345-0123	$10.00	75.0%	$7.50	60.0	$450.00
12345-0124	$20.00	75.0%	$15.00	29.4*	$441.18

* The 29.4 is calculated for the "0124" NDC-9 by weighting (at 72% and 28% respectively), Table A's average units per 30-DES (of 30 and 28 respectively).

Step 10: Weight the non-FAMP ceiling for each NDC-9 by the 30-day equivalent supply mix

Multiply the non-FAMP ceiling price for each NDC-9 by the share of total 30-day equivalent supplies dispensed associated with the NDC-9.

NDC-9	Non-FAMP Ceiling per NDC-9 [A]	30-DES Mix (%) [B]	Weighted non-FAMP Ceiling [A] x [B]
12345-0123	$450.00	71.8%	$323.20
12345-0124	$441.18	28.2%	$124.31

Step 11: Sum up the weighted non-FAMP ceiling prices across NDC-9s to establish one non-FAMP ceiling for the illustrative drug

Across both NDC-9s of the illustrative drug, the single non-FAMP ceiling price would be **$447.51**.

NDC-9	Weighted non-FAMP Ceiling
12345-0123	$323.20

12345-0124	$124.31
Total	**$447.51**

As a comparison, the steps below show that the same calculation as specified in § 429.435(a)(4) of the Proposed Rule results in a non-FAMP ceiling price for the same illustrative drug of **$448.65**. The steps below maintain the simplifying assumptions utilized above.

Step i: Non-FAMP per unit

The 5mg strength NDC-11 has an assumed non-FAMP per unit of $10.00, while the other two NDC-11s have assumed non-FAMPs of $20.00 per unit.

NDC-11	Non-FAMP per Unit
12345-0123-01	$10.00
12345-0124-01	$20.00
12345-0124-02	$20.00

Step ii and Step iii: Calculate a non-FAMP per unit across the year

For ease, the example will assume the non-FAMP per unit values in the table above apply across the full year.

Step iv: Calculate the weighted non-FAMP per unit for each NDC-11 by PDE unit mix

Calculate the non-FAMP per unit for each NDC-11 weighted by the PDE unit mix at the NDC-11 level.

NDC-11	Non-FAMP per Unit [A]	PDE Unit Mix by NDC-11 (%) [B]	Weighted non-FAMP per Unit [A] x [B]
12345-0123-01	$10.00	83.9%	$8.39
12345-0124-01	$20.00	11.6%	$2.32
12345-0124-02	$20.00	4.5%	$0.90

Step v: Grow calendar year 2021 calculation by CPI-U

For ease, the example will skip this step.

Step vi: Apply the applicable percent

Since this illustrative drug is a short-monopoly product, the applicable percent is 75%.

Step vii: Calculate the average non-FAMP ceiling per 30-day equivalent supply for each NDC-11

Multiply applicable percent from step vi by the weighted non-FAMP per unit for each NDC-11. Divide this product by the quotient of the total PDE units divided by average units per 30-day equivalent supply. Multiply these values together to get the non-FAMP ceiling per 30-day equivalent supply.

NDC-11	Weighted non-FAMP per Unit [A]	Applicable % [B]	Non-FAMP Ceiling per Unit [A] x [B] = [C]	Total PDE Units / 30-DES [D]	Non-FAMP Ceiling per NDC-11 [C] x [D]
12345-0123-01	$8.39	75.0%	$6.29	60.0	$377.42
12345-0124-01	$2.32	75.0%	$1.74	30.0	$52.26
12345-0124-02	$0.90	75.0%	$0.68	28.0	$18.97

Step viii: Sum up the non-FAMP ceiling prices across NDC-11s

NDC-11	Non-FAMP Ceiling
12345-0123-01	$377.42
12345-0124-01	$52.26
12345-0124-02	$18.97
Total	**$448.65**

If CMS were to modify the weighting in step iv above such that it relied on the 30-day equivalent supply product mix of, in this illustrative example, 71.8% for NDC 12345-0123-01, 19.9% for NDC 12345-0124-01, and 8.3% for NDC 12345-0124-02, the resulting non-FAMP ceiling price across all NDC-11's would be the same $447.51 as it was under section 60.2.3 of the IPAY 2028 Final Guidance. In other words, to maintain consistency with 60.2.3 and avoid a flawed single 30-day equivalent supply non-FAMP ceiling price, ***in § 429.435(a)(4)(iv) CMS should weight the non-FAMP ceiling per NDC-11 based on the 30-day equivalent supply mix, not the PDE unit mix***.

III. Temporary Floor for Small Biotech Drugs (§ 429.440).

PhRMA appreciates that CMS has recognized the possibility of a direct conflict between the statutory ceiling calculation and the Temporary Floor for Small Biotech Drugs. Section 1194(d) provides that, for an eligible small biotech drug selected for IPAY 2029 or 2030, the maximum fair price may not be less than 66 percent of the drug's 2021 average non-FAMP, adjusted for inflation. As CMS acknowledges, this provision can conflict with provisions governing the MFP ceiling.[134]

CMS proposes to resolve this conflict through an "adjusted ceiling." Under proposed § 429.440(b)(4), CMS would first disregard the 2021 non-FAMP amount specified in section 1194(c)(1)(C)(ii)(I) and calculate the non-FAMP component of the ceiling using only the more recent non-FAMP amount specified in section 1194(c)(1)(C)(ii)(II). If the resulting adjusted ceiling remained below the Temporary Floor, CMS would then raise the ceiling to equal the Temporary Floor, resulting in a single price that could be agreed upon as MFP.[135]

[134] 91 Fed. Reg. 36,236, 36,284–85.
[135] 91 Fed. Reg. at 36,284–85, 36,357–58.

We do not believe that this proposed approach represents the best reading of the statute. While CMS argues that its approach aims to give effect to both provisions of the statute, canons of statutory interpretation hold that the more specific provision controls.[136] In the IRA, Congress chose to specifically protect small biotech companies with a floor. This specific, targeted, and time-limited floor should be given its full force and effect by fully displacing the ceiling where the two conflict, rather than CMS inventing an extra-statutory "adjusted" ceiling price.

CMS itself appropriately characterizes section 1194(d) as establishing a "specific limitation to the general rules for MFP negotiations."[137] That characterization points to the proper resolution of the statutory conflict: only the specific protection– a floor – controls. A floor is a protection – establishing the bottom of a permissible range, not both the bottom and the top. Yet under proposed § 429.440(b)(4)(ii), if the adjusted ceiling remains below the Temporary Floor, CMS would make the floor and ceiling identical and permit only a single MFP.

That outcome would effectively convert Congress's Temporary Floor into a statutorily fixed price and eliminate any meaningful opportunity to negotiate above the floor based on the factors Congress directed CMS to consider under section 1194(e)—an outcome that is not envisioned by the general statutory scheme for "negotiation." The better reading is that Congress established the Temporary Floor as a minimum protection for the affected small biotech drugs as an exception to the ceiling price where that provision conflicts, leaving CMS and the manufacturer to negotiate an MFP at or above that minimum.

CMS states that selectively removing the 2021 non-FAMP amount is the most narrowly tailored way to preserve the ceiling calculation while giving effect to the Temporary Floor,[138] but the proposed approach does not preserve the ceiling calculation Congress enacted. Instead, CMS would intentionally decline to use the lower amount specified under section 1194(c)(1)(C)(ii) when the 2021 amount produces a ceiling below the Temporary Floor. Proposed § 429.440(b)(4)(i) would thus replace Congress's lower-of-two calculation with a one-number calculation that does not appear in the statute. ***CMS should revise proposed § 429.440(b)(4) to provide that, when the ceiling otherwise determined under § 429.410(b) or § 429.620(b) is below the Temporary Floor, the ceiling limitation does not apply and CMS must set an MFP not less than the Temporary Floor.***

[136] *RadLAX Gateway Hotel, LLC v. Amalgamated Bank*, 566 U.S. 639, 645 (2012) (quoting *Morales v. Trans World Airlines, Inc.*, 504 U.S. 374, 384 (1992)).
[137] 91 Fed. Reg. at 36,284.
[138] 91 Fed. Reg. at 36,284.

Appendix E: Negotiation Process (Subpart F)

The recommendations below focus on creating a more transparent, predictable and patient-centered negotiation process, including clearer standards for evidence evaluation, therapeutic alternatives and stakeholder engagement.

Key Recommendations:

- Allow a single global response for all manufacturer R&D costs and a single attestation for recoupment, with minimal weight placed on recoupment;
- Propose how the 1194(e)(1) factors will be considered and weighted, and confirm they will not be used to reduce prices;
- Provide a transparent explanation of how (e)(1) and (e)(2) factors are weighted and assign greater weight to patient-benefit factors;
- Provide greater transparency regarding the evidence relied upon in evaluating therapeutic advance, unmet need, and effects on specific populations;
- Exclude consideration of cost-effectiveness analysis from the MFP process and prioritize comparative clinical research and real-world evidence;
- Base therapeutic-alternative selection on the most clinically appropriate alternatives informed by patients, physicians, and manufacturers;
- Publish potential therapeutic alternatives when selected drugs are announced and allow stakeholder comment;
- Disclose methodology and assumptions used in therapeutic-alternative pricing calculations;
- Explicitly state the methodology for developing the starting point in the regulatory definition.
- Expand opportunities for stakeholder input and improve transparency into how that input influences decision-making.

I. Negotiation Factors (§ 429.505)

Section 1194(e)(1) (hereinafter referred to as the (e)(1) or manufacturer-specific factors) of the Social Security Act (SSA) describes the following manufacturer-specific data that CMS shall consider for purposes of setting the MFP of a selected drug: "(A) Research and development costs of the manufacturer for the medicine and the extent to which the manufacturer has recouped research and development costs;" "(B) Current unit costs of production and distribution of the drug;" "(C) Prior Federal financial support for novel therapeutic discovery and development with respect to the drug;" "(D) Data on pending and approved patent applications, exclusivities recognized by the Food and Drug Administration, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic Act or section 351(a) of the Public Health Service Act for the drug;" and ''(E) Market data and revenue and sales volume data for the drug in the United States."

In the Proposed Rule, CMS restates these factors essentially verbatim without providing meaningful detail on how it will collect or consider such information going forward. [139] In doing so, CMS has forgone

[139] § 429.505(b)(2).

the opportunity to simplify reporting and make data collection more feasible for manufacturers of selected drugs.

Research and Development Cost Recoupment

PhRMA continues to be concerned about the validity of CMS' approach to capturing "R&D recoupment," which does not account for all distribution and supply chain costs required to get products to market, among other concerns, and urges the Agency to acknowledge the concept's flaws and the difficulty of accurately quantifying and complying with it.

As PhRMA and others have continually noted, very few drug candidates that enter clinical trials are ultimately FDA-approved—just 12 percent in fact.[140] Companies plan R&D across entire portfolios, expecting that only a few successful drugs will generate enough revenue to offset the many costly failures.[141] To date, CMS' reporting instructions for R&D costs have been misaligned with how manufacturers actually track, allocate, and publicly report costs, creating significant compliance challenges under compressed timelines. Manufacturers cannot easily reconstruct highly detailed R&D costs for drugs developed over a decade or more ago, especially given CMS' overly broad definition of QSSD to include products approved under different applications. As a result, CMS' information collections requiring consideration of R&D costs at the product level and the extent to which R&D costs have been recouped is not only impractical but also unnecessary under the statutory language. CMS' fundamental misunderstanding of the economics of the biopharmaceutical marketplace exacerbates this flawed provision through the ongoing requirement for companies to report on R&D spending in ways not required by the IRA, such as providing detailed R&D costs and the extent to which they have been recouped, as well as by subdividing such costs into more than one subcategory. Furthermore, CMS' proposal to not allow Primary Manufacturers to report product acquisition costs for IPAY 2029 and beyond further restricts the scope of reportable R&D costs and disregards the fact that an acquiring company pays for the value of the R&D that was carried out to develop the selected drug, further adding to CMS' flawed approach to measuring R&D costs.

In the interest of simplifying reporting and providing predictability for future manufacturer reporting, PhRMA strongly recommends that CMS clarify in rulemaking that it will allow a single global response for all the manufacturer's R&D costs across all development programs, similar to a Form 10K for Securities and Exchange Commission filing, and a single attestation (YES/NO) for recoupment with the option to provide a supporting narrative. In addition, CMS should clarify in regulation that it will place minimal weight on recoupment and specify that it will not be used to reduce an MFP determined on the basis of a drug's therapeutic and clinical attributes.

CMS can simplify compliance and reporting for manufacturers regarding R&D dramatically by stating in binding regulations that, if a respondent stipulates "YES" that they have recouped research costs, then CMS will not and need not gather any additional information on these costs. If a manufacturer checks "NO," then the manufacturer should be allowed the flexibility to provide an explanation as to how the

[140] DiMasi J.A., Grabowski H.G., Hansen R.W. (February 2016). Innovation in the pharmaceutical industry: New estimates of R&D costs. *J Health Econ.* Available at: https://pubmed.ncbi.nlm.nih.gov/26928437/.
[141] Parry B., Moss R. (July 2024). Making more medicines that matter. *McKinsey and Company*. Available at: https://www.mckinsey.com/industries/life-sciences/our-insights/making-more-medicines-that-matter.

costs have not yet been recouped. This approach would accord with section 1194(e)(1)(A), which merely requires that CMS "consider" R&D costs and the extent to which they have been recouped. CMS could reason that in cases where a manufacturer stipulates it has recouped R&D costs, the agency would have no need to further include R&D costs in the MFP-setting analysis (as the costs have been recouped); whereas, in cases where the data show a manufacturer has not recouped R&D costs, such information may inform an upward adjustment to MFP.

Patents and Exclusivities

In the Proposed Rule, CMS provides no tangible details on how it will consider information on patents and exclusivities, as required by section 1194(e)(1)(D). The agency states:

> Patents and exclusivities may inform our understanding of therapeutic alternatives and other available therapy for the purposes of adjusting for clinical benefit, including consideration of the extent to which the selected drug represents a therapeutic advance or the extent to which the selected drug addresses an unmet medical need.[142]

CMS does not explain how this information may inform those considerations. It remains unclear how CMS may weight this information in relation to other factors and whether CMS would increase or reduce the preliminary price based on the described patents, exclusivities and marketing applications. ***PhRMA requests that CMS propose in new draft regulations how it intends to consider and weigh the 1194(e)(1) factors and confirm that it will not use these factors to reduce prices (at the very least, until stakeholders have the opportunity to comment on more granular proposals on how CMS will weigh and consider (e)(1) factors). Second, PhRMA urges CMS to clarify that it considers the data described in item D—i.e., pending and approved patent applications, exclusivities, and pending or approved marketing applications—as markers of a product's innovative nature, the investment that the manufacturer made in developing the product, and the lack of therapeutic alternatives, all of which are factors that weigh in favor of <u>increasing</u> the preliminary price.***

Providing Updates on Manufacturer-Specific Data

CMS proposes in § 429.505(c) that "if the Primary Manufacturer becomes aware that any . . . information has changed or is otherwise inaccurate" it must provide updates to the manufacturer-specific data "in a form and manner prescribed by CMS." First, APA requirements for notice-and-comment preclude CMS from incorporating open-ended standards in regulation – such as those citing to an as-yet unknown "form and manner" for reporting. Such "bootstrapping" violates the requirement that stakeholders be given an opportunity to comment on binding requirements to which they are subject, as commenters cannot predict exactly what "form and manner" CMS will mandate. Second, the requirement for continuous updates is confusing. Reporting may have been accurate – to the best of a submitter's knowledge – at the time of submission, and CMS does not explain why Primary Manufacturers must be subject to a vague and continual requirement for updating, how significant changes must be, or whether there are certain factors CMS is concerned with. Further, as discussed in our comments on subpart K, CMS proposes severe, immediately-imposed penalties for so-called "inaccurate" information, without offering a guaranteed corrective action opportunity. CMS should alter its rules (both in § 429.505(c) and in § 429.615) to

[142] 91 Fed. Reg. at 36295.

specify that these requirements govern only information where it becomes clear that such information was inaccurate *at the time of submission*. CMS should also delete open-ended standards throughout the regulation – such as requiring Primary Manufacturers to comply with as-yet unknown "form and manner" standards.

Emphasizing 1194(e)(2) Factors Related to Patient Benefit

Section 1194(e)(2) (hereinafter referred to as the (e)(2) factors) of the SSA allows all stakeholders to submit evidence on the selected drug's comparative effectiveness relative to therapeutic alternatives. In the Proposed Rule, CMS has provided no new details on how it will utilize the (e)(2) factors in calculating a product's MFP. The agency states its criteria in a manner so general as to provide almost no meaningful legal guidance at all, stating that "CMS uses a qualitative approach to broadly evaluate the body of available evidence related to section 1194(e)(2) factors … in totality, including any combination of" the 1194(e)(2) factors spelled out, without further detail, in the proposed regulation.[143]

The agency reaffirms in the proposed rule that it intends to employ a "two-pronged approach" to review of evidence on (e)(2) factors that involves CMS' own synthesis and evaluation of available evidence, as well as research submitted by manufacturers and other stakeholders. As noted in prior PhRMA comments to the Agency, the short timetables involved in the annual process for setting MFPs combined with the complexity of evidence reviews (e.g., in deciding on therapeutic alternatives, sources of evidence to include or exclude, and how different research and data are considered) make it particularly important for the agency to establish transparency as well as predefined protocols for the evidence identification and review process. As researchers have noted, a predefined evidence review protocol is a core best practice for evidence-based decision-making because it reduces the risk of subjectivity and bias, improves the reproducibility of findings, and provides stakeholders clarity regarding how evidence will be identified, selected, and assessed.[144] In addition, the IRA requires CMS to use a "consistent methodology and process."[145] Yet, CMS has not articulated an evidence review protocol. The proposed rule thus conflicts with the statute and represents a missed opportunity in this regard.

In addition, Sec. 1194(e)(2) specifies that CMS must consider evidence related to specific patient subgroups. CMS' evidence identification and assessment protocols developed should give particular attention to this issue, as well as patient-centered outcomes. MFP explanations released to date by CMS provide only limited information on how patient input or patient-centered outcomes were considered by the agency, which raises concern that they may be under-weighted or ignored. In fact, a review of three selected drugs in IPAY 2027 found that less than two percent of studies referenced by CMS in the MFP explanations described how patient involvement affected study design; and evidence about patient experience appeared in only ten to 16 percent of all data cited.[146]

[143] Proposed § 429.510(e).
[144] Mattingly T.J. II, Towse A., Garrison L.P. Jr. (October 2024). Robust Evidence Synthesis To Support Transparent Medicare Drug Price Negotiation. *Health Affairs Forefront*. Available at: https://www.healthaffairs.org/content/forefront/robust-evidence-synthesis-support-transparent-medicare-drug-price-negotiation.
[145] SSA § 1194(b)(1).
[146] Partnership to Improve Patient Care. (August 2026). Medicare Drug Price Negotiation – Is CMS Listening to Patients? Available at: https://www.pipcpatients.org/news/the-data-mine-medicare-drug-price-negotiation-is-cms-listening-to-patients

As PhRMA and other key stakeholders[147] have previously recommended, ***CMS should (a) provide a transparent explanation of how (e)(1) and (e)(2) factors are currently weighted; (b) assign a greater weight to (e)(2) factors as compared to the (e)(1) factors; and (c) within such (e)(2) factors, assign greater weight to those that actually reflect the benefit the selected drug brings to patients, caregivers, and society and will help encourage the generation of additional evidence on the comparative health benefits of different treatments.*** As a corollary, to the extent (e)(1) factors are considered, CMS should place less weight on the (e)(1) factors that would diminish medicines' benefits and could stagnate innovation if overweighted.

Basing prices for medicines on costs incurred by the manufacturer, instead of the value and benefits conferred by the innovation, sends perverse, unintended signals to manufacturers that devalue and disincentivize R&D, posing a significant threat to innovation and progress for future medicines. Manufacturers require a clear understanding as to whether innovation and progress will be valued under CMS' price setting framework. As such, ***CMS should provide greater transparency on the types of evidence it will rely on when evaluating data, such as the extent to which a selected drug represents a therapeutic advance or addresses an unmet medical need, and the effects of the selected drug on specific populations.*** Providing clarity in how CMS will consider evidence on a selected drug in regulation will provide greater certainty to manufacturers about the types of evidence they should develop and how they may expect MFPs to be calculated. CMS would also demonstrate a clear, lasting commitment to prioritizing patient benefit.

We appreciate the degree to which CMS' public explanations of MFPs provide some retrospective insight on the agency's incorporation of comparative effectiveness and patient-centered outcomes in its process.[148] However, greater prospective transparency in how such information will be incorporated into prespecified protocols would strengthen stakeholder predictability and public confidence in the process.

Quality-Adjusted Life Years

PhRMA appreciates CMS' recognition that current statute precludes the agency from considering research or evaluations involving the Quality-Adjusted Life Year (QALY) or similar cost-effectiveness metrics as part of policy decisions such as establishing final MFPs. However, we remain concerned that CMS proposes to continue considering other types of cost-effectiveness analysis (CEA) methods as well as other outcomes (such as relative health benefit or comparative clinical outcomes) that could be derived from CEA studies. Other types of CEA metrics incorporate flaws similar to those of the QALY, or trade the QALY's discriminatory design for other problems (such as devaluing quality-of-life gains). Further, there is a risk that CEA studies' economic objectives could exert influence and bias in the study's clinical design (such as selection of comparators, or how uncertainty in endpoints or evidence are interpreted). Finally, Sec. 1194(e)(2) does not reference CEA, instead focusing primarily on comparative clinical effectiveness, making consideration of CEA unnecessary. ***CMS should exclude consideration of CEA***

[147] McElwee F., Cole A., Garrison L.P., Towse A. (June 2024). Federal Support Should Not Be A Factor In Determining Pharmaceutical Prices Under The IRA. *Health Affairs Forefront*. Available at: https://www.healthaffairs.org/content/forefront/federal-support-should-not-factor-determining-pharmaceutical-prices-under-ira.

[148] Martin K., Sachs R. (March 2026). Understanding The Explanations For The 2027 Medicare Drug Price Negotiation Cycle. *Health Affairs Forefront*. Available at: https://www.healthaffairs.org/content/forefront/understanding-explanations-2027-medicare-drug-price-negotiation-cycle.

from the MFP process and prioritize comparative clinical research and other data that provides insight into a medicine's real-world performance, without undervaluing or discriminating against the lives of the elderly, the disabled, or the terminally ill.

II. Methodology for Developing the Initial Offer (§ 429.510)

Therapeutic Alternative Selection

Identification of therapeutic alternatives represents a critical element of the MFP process, yet it is also a notoriously difficult element of any process for evaluation of the comparative costs and benefits of different medicines or other health care interventions. CMS has not provided meaningful clarity on the evidence or process the agency uses to select therapeutic alternatives, a shortcoming from prior IPAY guidance that is retained in the proposed rule. This was illustrated by CMS' release of MFP explanations for the IPAY 2026 drugs, which indicate that the agency considered an average of six and a half therapeutic alternatives across each of the ten selected drugs (ranging from one to ten therapeutic alternatives per selected drug), but provided little specific information about how the agency ultimately selected specific therapeutic alternatives beyond vague statements on use of a "holistic" approach.[149] Selection of clinical comparators can be highly variable, raising questions about whether the decision was informed by other factors or objectives of the government's decision-making, rather than clinical appropriateness.[150]

As PhRMA has stated previously, therapeutic alternative selection should be based on the most clinically appropriate alternative informed by conversations with and data submissions from experts with real-world experience, including patients, practicing physicians and pharmaceutical manufacturer(s). However, the agency's extremely compressed timetable for input, combined with vague, poorly defined standards for therapeutic alternative selection, makes it exceptionally difficult for manufacturers and other stakeholders to efficiently provide meaningful input on a selected drug relative to its therapeutic alternatives, and raises the risk that CMS will not identify the most clinically appropriate options.

Through rulemaking, CMS has the opportunity to provide clear, rigorous and binding standards for how the agency identifies and utilizes therapeutic alternatives to calculate a product's MFP. In the Proposed Rule, CMS disappointingly provides no new clarity or specifics about how it will identify therapeutic alternatives, retaining the very general criteria used in previous guidance.

Without insight into CMS' development of therapeutic alternatives, manufacturers have no visibility into whether there are gaps or issues in the process, which could ultimately impact pricing, and limited time to develop analysis of how a selected drug compares with the therapeutic alternatives CMS ultimately identifies. ***CMS should commit in regulation to publishing the potential therapeutic alternatives under consideration for each selected drug when selected drugs are announced and allow data submitters to comment on CMS' proposal as part of their data submission package***. This would significantly reduce

[149] National Pharmaceutical Council. (January 2025). "Maximum Fair Price" Explanations for IPAY 2026 Drugs. Available at: https://www.npcnow.org/sites/default/files/2025-01/MFP%20Explanation%20Files%20IPAY%202026%20NPC%20Policy%20Evidence%20Brief%202025_01.pdf.

[150] Hernandez I. et al. (December 2023). Medicare drug price negotiation: The complexities of selecting therapeutic alternatives for estimating comparative effectiveness. *J Manag Care Spec Pharm*. Available at: https://pmc.ncbi.nlm.nih.gov/articles/PMC10909583/.

stakeholder burden by allowing data submitters to tailor their submissions to CMS and limit the potential scenarios stakeholders currently need to consider when preparing Information Collection Request (ICR) responses.

Starting Point for Initial Offer

PhRMA is concerned that the Proposed Rule does not provide sufficient clarity on how CMS will use therapeutic alternatives once they have been identified to determine the starting point for the initial offer. Although CMS' general approach to identifying therapeutic alternatives appears largely consistent with prior guidance, the Proposed Rule leaves substantial ambiguity regarding how CMS will translate therapeutic alternative prices into the starting point.

This ambiguity is especially problematic for multi-indication products and for products used across different lines of therapy, regimens, biomarker-defined populations and treatment settings. Without a required utilization-weighted and condition-level starting point methodology, CMS could allow a low-cost alternative relevant to only one FDA-approved indication, line of therapy, regimen or patient subgroup to exert disproportionate influence on the starting point for the entire selected drug.

PhRMA urges CMS to clarify in the final rule that, for selected drugs with therapeutic alternatives across multiple FDA-approved indications or conditions, CMS will calculate FDA indication-level therapeutic alternative starting points and weight those starting points based on the Medicare utilization of the therapeutic alternatives relative to the selected drug in the same relevant population. CMS should also clarify that indications with no clinically comparable therapeutic alternative, or with high unmet need, will be reflected in the condition-level starting point methodology and not addressed only through later 1194(e)(2) factor based qualitative adjustments.

CMS should further disclose, at or before the initial offer, which FDA-approved indications or conditions were included or excluded, the therapeutic alternatives used for each indication, the NDCs and HCPCS codes included, the Part B and Part D channels and claims periods used and the utilization weights applied to each therapeutic alternative and condition. If FDA-approved indications are excluded, CMS should provide a clinical rationale for doing so. These non-price methodological disclosures would not require CMS to disclose confidential therapeutic-alternative prices, but would provide manufacturers with information necessary to understand whether the starting point is clinically and economically representative of the selected drug's Medicare use and provide an informed and rational counteroffer.

PhRMA is also concerned that CMS' proposed tailored 30-day equivalent supply methodology for therapeutic alternatives could materially distort the starting point for selected drugs, particularly in therapeutic areas where therapies are used as part of multi-agent regimens, fixed-duration treatment courses, intermittent cycles, loading and maintenance phases, or sequential treatment pathways. This flexibility creates an important concern for selected drugs used in complex regimens. CMS could treat a low-cost agent, alone or as a component of a regimen, as the relevant therapeutic alternative for a selected drug-containing regimen even where the low-cost agent is not a clinically equivalent substitute for the selected drug. CMS could also use a tailored 30-day equivalent supply methodology to normalize short-cycle, intermittent, or fixed-duration low-cost agents in a way that makes the therapeutic alternative appear extremely inexpensive on a 30-day basis.

CMS should disclose, at or before the initial offer, whether it used the standard or tailored 30-day equivalent supply methodology for each therapeutic alternative; the NDCs and HCPCS codes included; the dosing, duration, cycle-length, treatment-course and utilization assumptions; and whether the methodology was applied to a single agent or a complete regimen. These disclosures are necessary to allow the manufacturer to evaluate whether CMS' therapeutic alternative pricing reflects a clinically comparable and complete course of care, rather than a low-cost component that does not represent a reasonable therapeutic alternative for the selected drug and call that error to CMS' attention.

PhRMA additionally reiterates its opposition to the use of alternative starting points for initial offers, such as those CMS states it considered in this rulemaking[151] and in the IPAY 2028 Draft Guidance, and we urge CMS to start with the statutory ceiling. We are especially concerned by consideration of a starting point between the price of the therapeutic alternative(s) and the "unit cost of production and distribution," or potential use of "domestic reference prices."[152] As noted above, this approach fails to consider the important clinical and quality of life benefits provided by MFP-selected medicines, and PhRMA appreciates that CMS has rejected these possibilities in the Proposed Rule. ***For the sake of clarity, PhRMA suggests that the definitions used for "starting point" in § 429.20 should explicitly and clearly state the methodology for developing the starting point, rather than define the term by reference to the price setting process description in § 429.510.***

III. Stakeholder Engagement (§ 429.515)

While PhRMA appreciates the efforts that CMS has made over time to improve stakeholder engagement with patients, caregivers, patient advocates and practicing physicians, the process as currently conducted still falls short of supporting meaningful patient engagement. For example, CMS frequently releases important information too late in its process, which prevents engagement. In the case of the stakeholder events, CMS failed to release the redacted transcripts from April 2025's events until over a month later in June, after CMS sent impacted manufacturers the Agency's initial offer for IPAY 2027. CMS also held its stakeholder events in the middle of a weekday, on short notice, placing a barrier on patients, caregivers, or practicing clinicians who needed to work or faced another type of conflict. By doing so, CMS severely limited who could participate and as a result, reduced the valuable insight that could impact CMS' evaluation of evidence and its MFP determination. Similarly, allowing these stakeholders only one month to complete the 1194(e)(2) section of the ICR—a timeframe that the Agency does not have to adopt under the statute—creates additional barriers for many stakeholders including those who are disabled, lack substantial resources or otherwise come from a disadvantaged background. CMS also continues to rely on a black box process that may discourage stakeholders from spending their time providing input that they fear the Agency will not take into consideration. Publicly released MFP explanations from both IPAY 2026 and 2027 largely included boilerplate statements, instead of providing stakeholders with any insight into CMS' process or the way in which the Agency incorporated patient-centered data or inputs.

While PhRMA appreciates that CMS may wish to preserve some flexibility to continue to adapt and expand opportunities for patient and other stakeholder input, the Proposed Rule is disappointing for its lack of specificity about such forms of engagement and how CMS will incorporate such information. CMS simply states, at proposed § 429.515(b), "CMS may hold event(s) in a form and manner and at

[151] 91 Fed. Reg. 36290.
[152] *Ibid.*

times to be specified by CMS to seek information from patients and other interested parties about selected drugs, therapeutic alternatives to the selected drugs, and other information."

CMS could, for instance, commit to holding certain baseline opportunities—such as multiple public meetings for stakeholder input per selected drug—that would demonstrate a commitment to stakeholder input while still preserving flexibility for the agency to experiment with expanding new formats for input. Importantly, committing to certain forms of stakeholder input, as well as certain ways in which CMS will consider such input, will provide predictability to stakeholder groups in coming years, giving them an incentive to prepare information for CMS to consider.

We urge CMS to continue to expand opportunities for soliciting stakeholder input and improve transparency into how this input influences the Agency's decision-making, and to incorporate some level of predictability regarding stakeholder input opportunities and the Agency's efforts to consider such input in rulemaking. Without fundamental improvements, CMS risks creating the impression of tokenism in which patient and clinician input is sought but not actually considered.

Appendix F: Renegotiation of an MFP (Subpart G)

The recommendations below seek to establish clear, predictable and administratively feasible standards for renegotiation eligibility, selection and data collection.

Key Recommendations:

- Confirm that Part B utilization for a drug originally selected as a Part D drug is not, standing alone a material change for renegotiation purposes;
- Clarify that a change in insurance coverage or reimbursement status is not, by itself, a change in unmet medical need and may not trigger renegotiation;
- Adopt an affirmative rule that recently selected drugs will not be selected for renegotiation absent a change in monopoly status or a manufacturer request;
- Reconsider the 15 percent magnitude criterion;
- Raise the threshold for a significant change to at least 35 percent;
- Align proposed § 429.615(b) with the draft ICR so manufacturers need only submit information that has changed since the last full submission.

I. Eligibility of Drugs for Renegotiation (§ 429.605)

Proposed § 429.610(a)(2) states that CMS will consider selected drugs from IPAY 2026 and 2027—"including those with Part B utilization"—for renegotiation eligibility under section 1194(f)(2) of the Act on the same footing as any other selected drug.[153]

PhRMA appreciates that the Proposed Rule, unlike some contradictory language in the IPAY 2028 draft guidance, does not suggest that Part B utilization is itself likely to render these drugs renegotiation-eligible or selected for renegotiation; instead subjecting the drugs to ordinary § 429.605 eligibility criteria. ***We ask CMS to make that treatment explicit and durable by confirming, in the final regulation text, that Part B utilization for a drug originally selected as a Part D drug is not, standing alone, a "material change" in any section 1194(e)(1) or (e)(2) factor for purposes of § 429.605(d).*** Part B utilization is not among the manufacturer-specific data elements enumerated in section 1194(e)(1) or the evidence about alternative treatments enumerated in section 1194(e)(2). Further, CMS' own material change standard turns on a *change* relative to the drug's most recent negotiation or renegotiation. Thus, certainly in cases where a drug's Part B utilization did not newly arise but existed before the relevant selection date for an IPAY, there has been no "change" in any sense under the statute or proposed § 429.605(d)(1). CMS should confirm this policy with an express statement in the final regulation text.

Additionally, Table 2 of the Proposed Rule illustrates CMS' proposed approach to determining a "material change" in a section 1194(e) factor.[154] The final illustrative scenario in that table describes an indication that "was not covered under Part D or payable under Part B at the time the drug was previously negotiated," is "now covered under Part D and/or payable under Part B," and for which "there are no alternative treatments available for that indication."[155] CMS states that in this scenario, the newly covered

[153] 91 Fed. Reg. at 36300. We note that the reference to § 429.610(a)(2) appears to be a typo as that specific regulatory citation does not appear in the proposed reg text.
[154] 91 Fed. Reg. at 36302.
[155] *Ibid* at Table 2.

indication "would meaningfully impact CMS' consideration of section 1194(e)(2)(D) of the Act," such that the change may be considered material.[156]

We are concerned this example conflates a change in insurance coverage with a change in unmet medical need. Proposed § 429.20 defines "unmet medical need" as "a circumstance in which the relevant disease or condition is one for which no other treatment options exist, or existing treatments do not adequately address the disease or condition," assessed based on all information available "at the time of consideration." That is a clinical definition: it asks whether adequate treatment alternatives exist for a disease or condition, not whether Medicare currently pays for a given medicine to treat it.

The Table 2 scenario, however, describes no change in the underlying clinical circumstance. By the scenario's own terms, no alternative treatments existed for the indication before the coverage change, and none exist after it. The only variable that changes is Medicare's payment status. Nothing about the disease, the condition or the available treatment landscape has changed. CMS' own regulatory definition in § 429.20 does not allow CMS to treat an "unmet medical need" as encompassing changes in insurance coverage. Nor would such an interpretation be consistent with the clinical focus of the section 1194(e)(2) factors generally.

We ask CMS to revise the Table 2 example, or otherwise clarify in the final rule, that a change in insurance coverage or reimbursement status is not, by itself, a change in unmet medical need under section 1194(e)(2)(D) and may not trigger a renegotiation.

II. Selection of Drugs for Renegotiation (§ 429.610)

Timeline for Renegotiation Eligibility

CMS acknowledges in the Proposed Rule that, for selected drugs negotiated or renegotiated only shortly before the applicable renegotiation-eligibility review, "the relatively short period" between the two events "may make it less likely" that such drugs would meet the material-change criteria proposed at § 429.610(b).[157] This is the same practical reality PhRMA raised in connection with the IPAY 2028 guidance: drugs selected for IPAY 2026 or 2027 will, under this Proposed Rule's timeline, be reviewed for IPAY 2029 renegotiation eligibility and selection only a short time after their MFPs were first set.

While we appreciate CMS' acknowledgment as a sound description of practical likelihood, it stops short of an operative commitment, leaving room for CMS to select such drugs on a case-by-case basis notwithstanding its own stated expectation. ***PhRMA urges CMS to adopt an affirmative rule: absent a change in monopoly status under § 429.605(b) or a request by the Primary Manufacturer itself, CMS shall not select recently selected drugs (such as those selected in the past two or three years) for renegotiation.*** Doing so would align CMS' regulations with what it has already stated in guidance and avoid subjecting manufacturers and CMS alike to a resource-intensive renegotiation process for drugs whose MFP CMS does not expect to change significantly.

[156] *Ibid.*
[157] 91 Fed. Reg. at 36304.

Threshold for a "Significant Change" in the MFP

Proposed § 429.610(b)(1) would establish a two-part, conjunctive test governing renegotiation eligibility when there is a new indication or a material change in an 1194(e) factor, per section 1194(f)(3)(C) of the Act. Under the proposal, CMS would select such a drug for renegotiation only where both (i) the change is likely to result in a 15 percent or greater change in the MFP, and (ii) that change would have a significant impact on the Medicare program.

PhRMA generally supports CMS' use of a conjunctive, two-factor framework—an approach that appropriately recognizes that financial magnitude alone cannot establish that a change is "significant" within the meaning of section 1194(f)(3)(C). We also urge CMS to consider, as part of the program-impact prong, not only spending and cost-sharing effects but whether the underlying change reflects greater clinical value to patients, and to maximize transparency in how "material change" determinations are made and documented. However, most importantly, PhRMA urges CMS to raise the threshold for determining whether an expected change in a drug's MFP would be "significant."

CMS should reconsider the 15 percent magnitude criterion, which sets the threshold at the floor of the range CMS' own methodology produces without justifying why that is the superior approach. CMS derived a 15 to 45 percent "informative range" from the percent change in the non-federal average manufacturer price (non-FAMP) applicable percentages that apply as a selected drug moves between monopoly-status tiers under section 1194(c)(3)(A)–(C) of the Act: a roughly 13.3 percent change (rounded to 15 percent) between short-monopoly (75 percent) and extended-monopoly (65 percent) status, and a roughly 46.7 percent change (rounded to 45 percent) between short-monopoly and long-monopoly (40 percent) status.[158] CMS chose the floor of that range, reasoning that a lower threshold better serves the statutory directive in section 1194(b)(1) of the Act to pursue the lowest possible MFP, and expressly rejected the 35 percent threshold that commenters proposed during the IPAY 2028 guidance cycle—reasoning that a percent-change methodology, rather than the arithmetic difference between applicable percentages, more faithfully tracks the statutory "significant change" language, and that a higher threshold risks "normaliz[ing]" sub-35-percent changes as immaterial.[159]

We disagree that this reasoning justifies defaulting to the *bottom* of CMS' own range. CMS' rationale addresses why a percent-change methodology is preferable to an arithmetic-difference methodology; it does not explain why, having adopted that methodology, CMS should select its lowest value rather than a threshold closer to the middle of the 15 to 45 percent band the methodology itself generates. Indeed, CMS' own analysis confirms that a 35 percent change "would fall in the range calculated based on the percent change in the applicable percentages"—meaning CMS' own framework already treats 35 percent as a defensible measure of a "significant" change, not an outlier requiring rejection.[160] An agency must supply a reasoned explanation connecting the facts found to the choice made, and reasoned decision-making requires more than establishing that the chosen figure is permissible; it requires explaining why that figure, rather than another figure equally supported by the agency's own data, was selected.[161]

[158] *Id.* at 36303.
[159] *Ibid.*
[160] *Ibid.*
[161] *See Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.,* 463 U.S. 29, 43 (1983).

Selecting the floor of a range, without addressing why the range's upper or middle values would not equally—or more faithfully—capture a "significant" change, does not reflect reasoned decision-making.

Practical considerations, both for the manufacturer and the Agency, reinforce the case for a higher threshold: A 15 percent trigger is likely to sweep in a substantially larger number of renegotiation-eligible drugs each cycle than a threshold closer to the middle of CMS' own range, increasing the administrative burden on both CMS and manufacturers and multiplying the number of concurrent offer and counteroffer proceedings CMS must administer consistent with its obligation to align renegotiation with the process established for initial negotiation under section 1194(b) of the Act. A threshold nearer the middle of CMS' 15 to 45 percent range would better conserve agency and manufacturer resources for those renegotiations most likely to yield a meaningful price change and would still fall comfortably within the range CMS itself has identified as capturing a statutorily "significant" change. ***We accordingly urge CMS to raise the threshold—at a minimum to 35 percent—and, if the 15 percent threshold is maintained as a minimum, to explain in the final rule why a figure at the floor of its own calculated range, rather than one nearer its midpoint, best satisfies section 1194(f)(3)(C)'s "significant change" standard.***

III. Data Collection to Inform Renegotiation Eligibility, Selection, and Renegotiation of the MFP for a Selected Drug (§ 429.615)

Burden of Mandatory Data-Submission on Manufacturers of Drugs Selected for Renegotiation

Proposed § 429.615(a) would maintain a voluntary submission mechanism by which Primary Manufacturers may provide information on new indications and updated section 1194(e) factors to inform renegotiation eligibility and selection. Proposed § 429.615(b)(1), however, requires that once a drug is selected for renegotiation, the Primary Manufacturer submit a full, updated set of section 1194(e)(1)-factor information—effectively the same data-elements submission required in original price setting process—on the same March 1 deadline applicable to initial submissions. This conflicts with CMS' Draft Information Collection Request for "Drug Price Negotiation for Initial Price Applicability Year 20XX under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10849, OMB 0938-1452)," which states that only information that differs from the Primary Manufacturer's most recent "full submission" of data is needed. If a Primary Manufacturer is not anticipating a drug being selected for renegotiation, it would be exceedingly difficult to complete the full request in the allotted 30 days.

CMS should align proposed § 429.615(b) with the draft ICR by inserting a statement in the proposed regulations that a manufacturer selected for renegotiation need only submit information that has changed from the last full submission. CMS also should consider identifying portions of the ICR that no longer require updates – such as market data and revenue and sales volume data, particularly given CMS' proposal to consider the MFP for purposes of developing the initial offer in a renegotiation. In that circumstance, the voluminous pricing metric data CMS initially collects is no longer relevant – as CMS is not basing prices on the market – but instead has chosen to employ price setting in Medicare as its metric.

In addition, for all data submissions (whether for the initial or re-negotiation), CMS should alter rules that require timely notification of changed or "otherwise inaccurate" information (such as in §§ 429.505(c) and 429.615(b)(2)) and request updates only if a submitter becomes aware that information was incorrect *as of the time of submission.* PhRMA explained in prior comments why CMS' vague standards for updates on "changed" information fails to recognize the ever-evolving nature of scientific inquiry.

Appendix G: Implementation of the MFP (Subpart H)

I. Application of the MFP Across Dosage Forms and Strengths (§ 429.700).

As discussed above, PhRMA has numerous concerns with CMS processes for the calculation of a single ceiling price and MFP based on a 30-day equivalent supply if applied to all medicines covered under Part D and all medicines covered under Part B.[162] While CMS' approach is appropriate for many medicines, and although CMS proposes workarounds for specific types of drugs administered a single time (such as vaccines, gene therapies and cancer therapies), the reliance on claims data to establish the 30-day equivalent supply can lead to undervaluing certain drugs, including those with fewer recurring administrations.

PhRMA also has concerns with the Agency's proposal to scale the MFP per unit and the MFP per billing unit based on price differentials across different dosage forms and strengths of the selected drug. An inaccurate and flawed 30-day supply methodology used at the outset of the process to determine a ceiling price and MFP cannot be relied upon as the basis for scaling that MFP across dosage forms and strengths. Instead, ***PhRMA urges CMS to adopt alternative methodologies that incorporate flexibility to determine a 30-day supply as explained in comments to Subpart E of the Proposed Rule; and to apply that methodology consistently through the application of MFP to different dosage forms and strengths***.

[162] See Comments to Subpart E.

Appendix H: Manufacturer Compliance and Oversight, and Civil Monetary Penalties (Subparts J & K)

The recommendations below focus on due process, transparency, corrective action opportunities and limits on enforcement authority.

Key Recommendations:

- Develop enforcement policies that stay within the constitutional and statutory limits, rely on effective communication with manufacturers and avoid imposing CMPs indiscriminately;
- Provide warning notices before CMPs begin to accrue;
- Provide an opportunity for corrective action and forgo CMPs when adequate corrective action is taken;
- Do not impose double CMPs for the same underlying conduct.

I. Civil Monetary Penalties

In subparts J and K of the proposed rule, CMS is proposing regulations on its approach to manufacturer oversight and enforcement, including under its authority to impose civil monetary penalties (CMPs) for certain violations under section 1197 of the Social Security Act. In developing its enforcement framework, it is critical that CMS focus on its obligation to abide by the constitution's due process requirements. The Due Process Clause of the Fifth Amendment prohibits the government from depriving persons of property "without due process of law."[163] In *FCC v. Fox Television Stations, Inc.*, the Supreme Court held that "[a] conviction or punishment fails to comply with due process if the statute or regulation under which it is obtained 'fails to provide a person of ordinary intelligence fair notice of what is prohibited, or is so standardless that it authorizes or encourages seriously discriminatory enforcement.'"[164] The Supreme Court similarly emphasized that "regulated parties should know what is required of them so they may act accordingly," and "precision and guidance are necessary so that those enforcing the law do not act in an arbitrary or discriminatory way."[165]

As explained in more detail below, we are concerned that each of the following proposals violates these due process guarantees. We urge CMS to alter these proposals in a way that ensures Primary Manufacturers are guaranteed due process and that CMS' monitoring and enforcement activities are fruitful in advancing CMS' stated goals. CMS describes its "primary goal" as "successfully administer[ing] all aspects of the Negotiation Program" and states that its enforcement activities should (among other things) "facilitate[] the ability to successfully engage in all components of the negotiation process within the established timeframes."[166] ***To further these goals, CMS must develop enforcement policies that stay within constitutional and statutory limits, rely on effective communication with manufacturers, and avoid imposing CMPs in an indiscriminate fashion.***

Revision of Proposed Regulatory Language at 42 C.F.R. § 429.900(c) to Provide Specific Notice of What Conduct Could Prompt Imposition of a CMP

[163] U.S. Const. amend. V.
[164] *FCC v. Fox Television Stations, Inc.*, 567 U.S. 239, 253 (2012) (quoting *United States v. Williams*, 553 U.S. 285, 304 (2008)).
[165] *Fox Television Stations, Inc.,* 567 U.S. at 253.
[166] 91 Fed. Reg. at 39314, 39315.

Under proposed 42 C.F.R. § 429.900(c), if CMS:

> concludes that the Primary Manufacturer is noncompliant with **one or more of the requirements of the Negotiation Program Agreement, including all applicable requirements and conditions set forth in sections 1191 through 1198 of the Act and all applicable guidance and regulations, including this part, implementing those provisions and any changes to the Act that affect the Negotiation Program**, CMS may take one or more of the following actions: (1) Provide a written notice to the Primary Manufacturer of the violation(s). (2) Request the Primary Manufacturer take specific corrective action to address the noncompliance, in a form and manner, and by the deadline specified by CMS. (3) Impose a [CMP] on the Primary Manufacturer as set forth in subpart K of this part.[167]

This proposal does not contain enough detail to "provide a person of ordinary intelligence fair notice of what is prohibited."[168] Instead, CMS provides a broad and vague range of sources of violations that could result in imposition of a CMP. For example, CMS refers to being "noncompliant with one or more of the requirements of . . . all applicable guidance and regulations" without specifying which guidance or regulations it is referring to, whether CMS purports to bind manufacturers to future unknown guidance, or what requirements in the guidance or regulations could lead to a CMP for failure to comply. This is particularly concerning because of the reference to "guidance"—undefined—which can take numerous forms.

Furthermore, because the proposed language is not clear about what is prohibited, it is not sufficient to ensure "that those enforcing the law do not act in an arbitrary or discriminatory way."[169] Without a clearer list of what could lead to a CMP, there is a risk that CMS could apply CMPs in an arbitrary or discriminatory way or could impose CMPs for an act or omission that a manufacturer may have no reason to identify as a violation of its obligations. Thus, if finalized as proposed, the regulatory language would violate basic principles of constitutional due process. CMS must fix this constitutional violation by more clearly identifying what conduct could result in a CMP and allowing a subsequent round of comment on such proposals.

Warning Notice Prior to CMP Accrual

Proposed 42 C.F.R. § 429.1005(d) states that "[w]hen a [CMP] is imposed under this section, CMS sends a notice to the Primary Manufacturer in accordance with § 429.1020(a) ***after*** the [CMP] stops accruing under § 429.1005(c)."[170] The preamble to the proposed rule makes this same point, and suggests that the idea of sending a notification to the manufacturer only after a penalty has started, accrued over time, and finally stopped accruing is actually what CMS intends—not merely a poorly drafted proposed regulation. For example, CMS states in the proposed rule preamble that:

[167] 42 C.F.R. § 429.900(c) (proposed) (emphasis added).
[168] *Fox Television Stations, Inc.,* 567 U.S. at 253.
[169] *Fox Television Stations, Inc.,* 567 U.S. at 253.
[170] 42 C.F.R. § 429.1005(d) (proposed) (emphasis added)

> [W]here a [CMP] is pursued, we intend to send a written [CMP] notification . . . that reflects the start date of the penalty accrual, the end date of the penalty accrual, and the total amount of the penalty assessed . . . In [an] earlier example, the start date of the penalty accrual would be the day after the applicable submission deadline. . . . [T]he [CMP] shall accrue until the Primary Manufacturer has provided the necessary information or otherwise taken any corrective action determined by CMS to be necessary to address the violation. . . .[171]

Neither CMS nor the manufacturer would benefit from penalties accruing while the manufacturer has not been informed that CMS believes it to be in violation, and therefore may not even have the information it needs to correct the situation promptly. This is especially concerning for Primary Manufacturers because the information collection request (ICR) questions that may trigger the CMPs at issue here are voluminous, not always clear, must be fully addressed within 30 days post-selection, and often seek information well beyond what is needed for CMS' price setting activities. Accordingly, even if CMS revises the regulatory language in 42 C.F.R. § 429.900(c) as described above, Primary Manufacturers may not have notice that CMS believes they violated a requirement until after the CMP stops accruing. This does not accord with basic due process, which requires that regulated parties "know what is required of them."[172] In addition, waiting until CMP accrual ends could result in a violation not being remedied for a much longer time than it would have been had CMS issued a warning notice, because the Primary Manufacturer may have no idea that CMS believes it violated a requirement.

Furthermore, it is unfair to make a Primary Manufacturer pay a larger CMP than it otherwise would have owed if it had received a warning notice and took corrective action based on that notice. CMS recognized in a similar context, relating to providing a warning notice and opportunity for corrective action for hospital price transparency requirement violations, that:

> By complying with the requirements, a hospital can avoid financial penalties. [The agency] also note[d] that hospitals determined to be noncompliant, and subject to a CMP, can avoid accruing larger amounts of CMPs by coming into compliance with the requirements.[173]

Thus, CMS itself has acknowledged the benefits of providing a prompt warning notice that enables a manufacturer to take corrective action and stop CMP accrual. Needlessly extending a period of noncompliance only hurts the manufacturer and CMS. ***Accordingly, we urge CMS to abandon this approach in the final rule and instead provide a warning notice to Primary Manufacturers before CMPs begin to accrue.***

Opportunity for Corrective Action Before Imposing CMPs

The preamble to the proposed rule states that under CMS' proposed enforcement approach, CMS may respond in one of several ways when it believes a manufacturer has violated its obligations: CMS may issue a corrective action request and forgo CMPs if the manufacturer takes corrective action; "determine

[171] 91 Fed. Reg. at 36315.
[172] *Fox Television Stations, Inc.,* 567 U.S. at 253.
[173] 84 Fed. Reg, 65524, 65588 (Nov. 27, 2019).

that, even if a Primary Manufacturer complies with a request for corrective action, it remains appropriate to issue a violation notice and impose a CMP for the initial violation"; or "may not issue a request for corrective action and instead send a notice of violation to the Primary Manufacturer and impose a CMP." We have several concerns about this proposal.

First, it is illogical to allow violative behavior to continue without attempting to prompt Primary Manufacturers to correct the violation. By enabling violative behavior to continue, CMS may be harming itself as well as the Primary Manufacturer and other parties. For example, CMS may lack information it needs for the MFP-setting process, which could potentially delay completion of the process.

Second, CMS itself previously stated that it would provide an opportunity for corrective action. For example, in the IPAY 2026, 2027, and 2028 guidance documents CMS stated that it "will provide Primary Manufacturers with an opportunity for corrective action in the event a submission is incomplete or inaccurate."[174] Although CMS recognizes that it is "not proposing to codify the policies previously stated in section 40.2.3 of the Negotiation Program Guidance," it does not explain why it is retreating from its decision to provide an opportunity for corrective action as a matter of course.[175] As the Supreme Court has held, when an agency changes a policy, "a reasoned explanation is needed for disregarding facts and circumstances that underlay or were engendered by the prior policy."[176] Here, CMS provides no explanation, let alone a "reasoned" explanation for why it has decided to change its policy regarding providing a default opportunity for corrective action.

Furthermore, in other situations CMS has chosen to provide an opportunity for corrective actions before imposing CMPs, even in cases where the underlying statute or regulation does not require it. For example, as discussed above, in relation to hospital price transparency requirements under section 2718(e) of the Public Health Service Act, CMS provides an opportunity for corrective action before considering CMPs. In the preamble to the final rule adopting the regulations that provide an opportunity for corrective action, CMS explained that it:

> anticipate[s] that hospitals would have the opportunity to take corrective action prior to the imposition of a penalty. . . . [P]rior to imposing a CMP on a hospital, we anticipate issuing a written warning notice and requesting a CAP from the hospital as initial steps to promote compliance. . . . By complying with the requirements, a hospital can avoid financial penalties. We also note that hospitals determined to be noncompliant, and subject to a CMP, can avoid accruing larger amounts of CMPs by coming into compliance with the requirements. [177]

As CMS highlights, providing an opportunity for corrective action allows regulated entities to respond and avoid accruing larger amounts of CMPs. Thus, in addition to fixing violative conduct, an opportunity for corrective action allows entities that may have inadvertently violated a requirement to avoid unnecessary additional expense. This point is particularly important where the context is a statute authorizing a one million dollar a day penalty—without any intent requirement—if a manufacturer is "in

[174] *See, e.g.*, IPAY 2028 Final Guidance § 40.2.3.
[175] 91 Fed. Reg. at 36315.
[176] *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 516 (2009).
[177] 84 Fed. Reg. at 65588.

violation of a requirement imposed pursuant to section 1193(a)(5) [requirements 'determined by the Secretary to be necessary for purposes of administering the program and monitoring compliance with the program'], including the requirement to submit information pursuant to section 1193(a)(4)."[178] It is unfair and unnecessary to impose penalties of this magnitude on a manufacturer that may have merely interpreted CMS' convoluted ICR form in a manner that differed from CMS' interpretation.

Similar to the hospital transparency requirements, CMS provides an opportunity for corrective action in relation to the mandatory insurer reporting provisions added to the Medicare Secondary Payer Act by Section 111 of the Medicare and Medicaid SCHIP Extension Act of 2007 (P.L. 110-173). These provisions authorize CMS to impose CMPs on non-group health plan (NGHP) responsible reporting entities (RREs) for late or deficient reporting. In the final rule implementing these provisions, CMS built several pre-penalty opportunities into its enforcement process, explaining in the final rule preamble that:

> it is not [the agency's] intent to penalize RREs for honest, infrequent mistakes, but instead to only resort to penalty when an RRE fails to report or submits reports in an untimely manner. . . . It is, therefore, CMS's shared opinion with commenters that the focus shall not be to punish and impose consequences **but instead to motivate proper reporting and maintain compliance with existing statute and regulation**. . . . **RREs will also be able to avail themselves of the informal notice and dispute process to alert CMS to their "good faith efforts" to report any records that CMS has identified as being out of compliance**.[179]

These examples demonstrate that CMS itself recognizes the importance of providing a pre-penalty opportunity for corrective action in terms of promoting compliance.

Third, it would be unfair to impose a CMP without providing an opportunity for corrective action given how burdensome and complicated the data reporting requirements are for Primary Manufacturers. Given the amount of data that must be submitted to CMS within an aggressive timeline, how dense the ICR form is, how strict the response character limits are, and the fact that CMS often requests data in a manner that is unclear to manufacturers, there are numerous ways a Primary Manufacturer completing the form in good faith could mistakenly omit required data or report data that they believe is accurate but that ultimately proves erroneous—or that CMS assesses as erroneous. Indeed, the combination of the compressed reporting schedule, the often-confusing reporting requirements and the format in which the questions are posed to Primary Manufacturers could almost entrap manufacturers into submitting responses that CMS would deem to violate a manufacturer's information-submission obligations. And thus, these features are also a trap for million-dollar-a-day CMPs if Primary Manufacturers cannot correct what CMS thinks of as a violation before a CMP is levied. It would be entirely unfair to impose a CMP on Primary Manufacturers given these circumstances without providing an opportunity for corrective action.

Fourth, not providing an opportunity for corrective action violates due process. As explained above, "regulated parties should know what is required of them so they may act accordingly."[180] Here, given how

[178] SSA § 1197(c).
[179] 88 Fed. Reg. 70348, 70364 (Oct. 11, 2023) (emphasis added).
[180] *Fox Television Stations, Inc.,* 567 U.S. at 253.

unclear the ICR questions Primary Manufacturers must answer can be and the lack of any intent requirement in SSA § 1197(c), an opportunity for corrective action is needed to enable Primary Manufacturers to "act accordingly" once they receive notice of what is required of them (i.e., through a warning notice). Absent such an opportunity, CMS could impose a CMP without a Primary Manufacturer having an opportunity to act based on a clear understanding of what is required of them, in violation of due process.

For these reasons, we urge CMS, in its final rule, to provide that it will not only send a warning notice prior to CMP accrual beginning, but will also provide Primary Manufacturers with an opportunity for corrective action and forgo CMPs if the manufacturer takes adequate corrective action.

Imposition of Two Penalties for the Same Underlying Conduct

CMS proposes that if it:

> send[s] the Primary Manufacturer a request for corrective action and the Primary Manufacturer does not comply with such request, in accordance with proposed § 429.900(c) [regarding noncompliance with 'one or more requirements of the Negotiation Program Agreement, including all applicable requirements and conditions set forth in sections 1191 through 1198 of the Act and all applicable guidance and regulations, including this part, implementing those provisions and any changes to the Act that affect the Negotiation Program'] [CMS] may issue a violation notice and impose a CMP **for the failure to comply with CMS' corrective action request, which would be separate from any violation notice and CMP imposition addressing the violation that arose from the Primary Manufacturer's initial [violation]**.[181]

Not only does the above excerpt highlight CMS' policy that a Primary Manufacturer may be subject to civil monetary penalties for the actions of secondary manufacturers they do not control, but under this proposal, CMS could also seemingly impose not just one, but ***two*** penalties for the same underlying conduct. This directly contradicts the language of the statute which provides for the imposition of "***a*** civil monetary payment," not two CMPs, for the enumerated violations.[182] Further, in the case of a manufacturer failing to provide the complete information that CMS requires, this proposal would turn the words "[a manufacturer] shall be subject to a [CMP] equal to $1,000,000 for each day of such violation" into the words "[a manufacturer] shall be subject to a [CMP] equal to $2,000,000 for each day of such violation." CMS cannot read into the statute more CMPs than Congress authorized.

Not only is it fundamentally unfair to impose two penalties for the same underlying conduct, it is particularly unfair to do so here. As discussed above, one of the violations for which CMS can impose CMPs is failure to submit required data. However, the questions that Primary Manufacturers must answer when submitting data are not always clear and a Primary Manufacturer could legitimately interpret a question in a different way than CMS, resulting in CMS determining that the Primary Manufacturer failed to submit required data. And in turn, CMS could send a request for corrective action that the Primary

[181] 91 Fed. Reg. at 36315 (emphasis added).
[182] *See, e.g.*, SSA § 1197(b), (c) (emphasis added).

Manufacturer cannot satisfy despite its best efforts because it cannot gather the data needed by CMS' mandated deadline. In such a situation, under CMS' proposal, the Primary Manufacturer could be subject to duplicative CMPs despite the Primary Manufacturer's best efforts to remedy its initial violation. And a manufacturer's failure to provide information sought by CMS is still the same failure once CMS explicitly seeks the information and advises the manufacturer of the need for corrective action.

CMS previously stated that, in relation to a Primary Manufacturer's failure to provide complete and accurate data, it may issue a CMP "initially ***or*** in response to CMS' initial questions ***or*** Request for Corrective Action."[183] CMS provides no explanation for why it now plans to impose a CMP for both the initial violation and the failure to respond to a request for corrective action on time. As discussed above, when changing a policy, agencies must provide "a reasoned explanation . . . for disregarding facts and circumstances that underlay or were engendered by the prior policy."[184] Here, CMS again violates this principle by providing no explanation for why it has decided to change this policy.

Moreover, as explained above, prior to receiving a warning notice and an opportunity for corrective action, a Primary Manufacturer may not have had adequate notice of what act or omission CMS considered a violation. This lack of notice, followed by two-million-dollars-a-day penalties, violates due process and departs from the text of SSA § 1197. ***Thus, we urge CMS to provide in the final rule that CMS will not impose double CMPs for a manufacturer violating an obligation and failing to correct the same violation within a timeframe specified by CMS.***

[183] IPAY 2028 Final Guidance § 40.2.3 (emphasis added).
[184] *FCC v. Fox Television Stations, Inc.*, 556 U.S. at 516.

Appendix I: Proposed Implementation of Inflation Reduction Act Provisions for the Medicare Prescription Drug Benefit Program

I. Technical Comment on Proposed Amendments to § 423.120

CMS proposes to update 42 C.F.R. § 423.120 to include the requirement that each Part D drug that is a selected drug for which an MFP is in effect must be included on formularies. ***The regulation should be updated to reflect the rule CMS states in preamble***, that: "because a selected drug includes all dosage forms and strengths to which the MFP applies, section 1860D–4(b)(3)(I)(i) of the Act requires that formularies include all such dosage forms and strengths of the selected drug that constitute a covered Part D drug and for which the MFP is in effect."[185] Specifically, the language, "include each Part D drug", in proposed § 423.120(b)(2)(vii) should be replaced with "include all dosage forms and strengths of each Part D drug". This will ensure that CMS' interpretation has the force and effect of law and is included in the regulatory text governing the Part D program.

II. Part D Access and Coverage

PhRMA reiterates our comments in Appendix C to our comments on CMS' Draft Guidance for IPAY 2028, 2027 and 2026, submitted on June 26, 2025. In these comments, we expressed concern that CMS' existing formulary review process may not be sufficient to protect patient access and recommended CMS adopt stronger oversight and safeguards to protect beneficiary access in three key areas:

- **Improving transparency and data collection**. CMS should require Part D sponsors to report data that will provide critical transparency into the true impact of coverage denials on Part D beneficiaries, and develop meaningful, patient-centered ways of holding plans accountable for ensuring medication access. This is especially critical considering new analysis showing that among the first ten drugs selected for price setting, denial rates remained largely unchanged after the price controls took effect, with initial rejection rates for immunology and oncology reaching 59 and 67 percent respectively.[186] PhRMA provided detailed specifications for recommended data collection in our comments in response to the 2027 Part C and D Reporting Requirements ICR.[187]
- **Enhancing patient access safeguards.** CMS should ensure all prior authorization (PA) requirements are accessible to all stakeholders, require plan sponsors' utilization management (UM) determinations to "follow" the patient, update Medicare Plan Finder (MPF) to require plans to clearly display specific UM requirements and require plans to allow beneficiaries to initiate coverage determinations directly at the pharmacy counter. Further, CMS should ensure appropriate use of MA plans' use of step therapy for Part B drugs, given the inclusion of Part B drugs in IPAY 2028.
- **Strengthening formulary review reporting.** CMS should monitor and publicly report on formulary trends across all Part D plans and ensure the average number of medicines covered per class does not decrease. Recent research found that Medicare coverage for drugs in

[185] 91 Fed. Reg. at 36319.
[186] IQVIA (August 2026). Rejection Rates Unchanged by MFP Drug Coverage Requirement. Available at: https://www.iqvia.com/locations/united-states/blogs/2026/07/rejection-rates-unchanged-by-mfp-drug-coverage-requirement
[187] *See* https://www.regulations.gov/comment/CMS-2026-0958-0047.

competitive classes declined in 2025 and 2026, with average coverage falling 11.8 percentage points for PDPs and 5.8 percentage points for MA-PDs.[188]

[188] Zheng H., et. al. (July 2026). Changes in Medicare Part D coverage in competitive classes in the post–Inflation Reduction Act landscape: 2024–2026. *Health Affairs Scholar.* Available at: https://doi.org/10.1093/haschl/qxag171