April 14, 2023

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

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

Dear Administrator Seshamani:

In response to the Centers for Medicare & Medicaid Services' (CMS) "Drug Price Negotiation Program Guidance: Initial Memorandum, Implementation of Section 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments", Incubate submits the below comments to express our concern that the guidance does not consider industry warning signs and will have a detrimental impact on future investment in the life sciences, ultimately to the detriment of patients.

Incubate is a coalition of early-stage life sciences venture capital firms representing the patient, corporate, and investment communities. Our primary aim is to educate policymakers on the role of venture capital in bringing promising treatments to patients in need.

CMS Doubles Down on Price Controls

Since passage of the Inflation Reduction Act (IRA) in August 2022, Incubate has sounded the alarm that the law creates significant uncertainty for the life sciences investor community and upends the successful ecosystem of biopharmaceutical investment, research, and development that has enabled the United States to lead the world in developing new drugs. A number of investors and companies have already shifted resources away from developing small molecule medicines and pursuing post-approval research in light of the IRA.[1]

We are disappointed that despite the opportunity to correct the law's ambiguity, CMS' initial implementation guidance lacks transparency in the price setting process and does not address fundamental issues created by the law.

Lacks Transparency in the Price Setting Process

In this guidance, CMS did not address the significant confusion with the implementation of the law in a way that would protect incentives towards innovation. The Agency did not consider mitigating the law's impact and, in fact, doubled down on problematic components of this law.

[1] Incubate Coalition. (n.d.). Life Science Investment Tracker. Retrieved April 14, 2023, from https://incubatecoalition.org/life-science-investment-tracker/

One example is CMS' very broad interpretation of what forms of a drug should qualify for price setting. CMS is choosing to apply the maximum fair price (MFP) to all forms of a drug with the same active ingredient or active moiety, even if they are completely new forms (e.g., IV vs. subcutaneous), approved under different product applications at the FDA, and regardless of whether all the forms meet the age requirement for an eligible drug. Investors continue to be concerned about the broad application of MFP, which will drive less investment and development.

Disincentivizes Small Molecule Drug Development & Post-Approval Research

The guidance also reinforces the IRA's perverse incentive to invest in biologics, instead of the development of small molecules. As we have noted previously, the standard 14-plus year calculation, established by a combination of patents and exclusivities, that venture capitalists rely on to recoup their investments, has shifted under this law to provide a larger reward for the development of biologics (13 years) than the development of small molecules (nine years).[2] The larger reward for biologics, ensured by the additional four-year exemption from price setting, penalizes small molecule development.

Small molecule drugs offer enormous benefits, both to patients and the health system, especially when they become inexpensive generics. These are not just the pills of yesterday. Small molecule drugs, some of which can cross the blood-brain barrier, offer hope for neurological diseases like Alzheimer's and brain cancer, which was highlighted in President Biden's Cancer Moonshot effort. Understanding the simple economic principle that capital will be allocated in the direction of the biggest risk-adjusted reward, we can anticipate fewer investments in small molecule medicines, which will be detrimental to patients.

We are also concerned that this guidance will discourage drug makers and venture capitalists from pursuing new uses for existing drugs through post-approval or secondary indications. The guidance specifically references how extending patents and exclusivities could directly lower MFP calculations:

> "In considering element (4) on patent applications, exclusivities, and applications and approvals for the selected drug, CMS intends to consider the length of the available patents and exclusivities before the selected drug may no longer be single source. For example, if the selected drug has patents and exclusivities that will last for a number of years, CMS may consider adjusting the preliminary price downward."[3]

The IRA's price-setting timelines already signaled to drug developers that they not follow the science, as any returns on investment will get cut off before new uses for medicines are developed. Under CMS' guidance, companies will now be penalized for successfully innovating new uses by lowering the preliminary price if there are existing patents and exclusivities on a drug. As a result,

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[2] Stanford, J. March 6. Congress must fix IRA small-molecule penalty. Stat News, https://www.statnews.com/2023/03/06/congress-must-fix-ira-small-molecule-penalty/.

[3] Centers for Medicare & Medicaid Services. (2021). Medicare Drug Price Negotiation Program: Initial Guidance. Retrieved April 14, 2023, from https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf

we expect research and development efforts towards secondary indications will decrease, thus limiting the investment and exploration of new or alternative applications of medical discoveries - which are critical for continued R&D in sectors like cancer.

Distorted Calculation of the MFP

The investor community is also unsettled about the opacity around the MFP calculation. Under CMS' guidance, there will be no understanding of the justification of the 2026 MFPs until after the next group of drugs are selected for negotiation. Disconcertingly for investors, there is also no visibility into CMS' process for their calculation.

In addition, all of the valuable contributions to raise an MFP are not being taken into account. We ask that the Agency consider the clinical, patient, and societal benefits of a drug when determining the calculation of MFPs. CMS does not currently take these variables into account, despite them significantly contributing to the value of the drug. We urge CMS to allow these variables to increase the MFP.

Perverse Signal to the Market

Finally, I must underscore the most concerning signal that this rule sends to the market: that following the science will not to be rewarded moving forward. Our current life sciences ecosystem – one that made the United States the top drug developing nation in the world – has previously operated by pursuing science first. This rule sends a signal to both innovators and investors that some discoveries are more valuable than others, and that some should not be further developed. If not corrected, we are fearful of the long-term ramifications on American biopharmaceutical discovery.

Thank you for your consideration in these comments, please do not hesitate to contact John@incubatecoalition.org for additional information.

Sincerely,

John Stanford
Executive Director
Incubate