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COMMENTS OF ITIF

to the

Centers for Medicare & Medicaid Services (CMS)

Washington, D.C.

In the Matter of: Request for public comment on selected drugs for the second cycle of negotiations under the Medicare Drug Price Negotiation Program	)	Medicare Drug Price Negotiation Program Public Engagement Events

February 27, 2025

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OVERVIEW AND BACKGROUND

ITIF submits the following comments to the Centers for Medicare & Medicaid Services (CMS) in response to its request for public comment on the next 15 drugs to become subject to government price setting as part of the Inflation Reduction Act.[1]

In August 2022, the Biden administration signed into law the Inflation Reduction Act (IRA), the first law in American history to grant the Centers for Medicare & Medicaid Services (CMS) the authority to control the prices of drugs. Specifically, it allows CMS to "negotiate"—although this effectively means to set—prices for specified drugs covered under Medicare Part B, outpatient care, and Medicare Part D prescription drug coverage.[2]

Studies show that such regulations harm the development of important treatments and cures in the long run. A 2021 report finds that the impact of price controls proposed by the IRA would result in a 29 to 60 percent decrease in pharmaceutical research and development (R&D) between 2021 and 2039, translating into between 167 and 342 fewer new drugs, and a loss of life in the next decade 20 times larger than that from COVID-19 in the United States between March 2020 and September 2021.[3] A 2024 study also found that proposals to extend price setting to all pharmaceuticals, while having immediate benefits for low-income and elderly populations, would dramatically reduce firms' investments in highly welfare-improving R&D for future biopharmaceutical innovation.[4]

Further, a RAND report which conducted simulations found that price controls that reduce pharmaceutical company revenues by 20 percent would result in a negative long-term per capita net present value, as measured by the monetary value of life expectancy minus the value of medical and drug spending. The

[1] Centers for Medicare & Medicaid Services, "Medicare Drug Price Negotiation Program Public Engagement Events," website accessed February 27, 2025, https://www.cms.gov/inflation-reduction-act-and-medicare/medicare-drug-price-negotiation/2027-public-engagement-events; CMS,"Requested Link - Medicare Drug Price Negotiation Program Public Submission Form," https://hpms.cms.gov/app/ng/pblc_cmt/.

[2] Juliette Cubanski, Tricia Neuman, and Meredith Freed, "Explaining the Prescription Drug Provisions," KFF, (2023), https://www.kff.org/medicare/issue-brief/explaining-the-prescription-drug-provisions-in-the-inflation-reduction-act/.

[3] Tomas J. Philipson and Troy Durie, "The evidence base on the impact of price controls on medical innovation" (working paper, Becker Friedman Institute, University of Chicago, 2021), https://bfi.uchicago.edu/wp-content/uploads/2021/09/BFI_WP_2021-108.pdf.

[4] Kate Ho and Ariel Pakes, "Evaluating Pharmaceutical Policy Options" (working paper, National Bureau of Economic Research, 2024), https://kateho.scholar.princeton.edu/sites/g/files/toruqf4136/files/documents/HoPakes_061524.pdf.

analysis concluded that imposing price controls offers modest benefits to the current generation but potentially very high costs to future ones.[5]

PRICE SETTING ADVERSELY AFFECTS BIOPHARMACEUTICAL INNOVATION

Beyond the impact of price controls on new drugs, a December 2023 report from the U.S. Chamber of Commerce finds that price controls could also substantially decrease funding for clinical trials. A reduction in clinical trials would mean fewer novel therapies, including for conditions such as heart disease and cancer, the leading causes of death in the United States. A comparison between the United States and a sample of leading Organization for Economic Cooperation and Development (OECD) countries with similar scientific strengths but stricter price controls revealed that the United States consistently outperforms the OECD average in terms of clinical trial activity and overall life-sciences innovation. This disparity further widens in early-phase clinical trial research, where the U.S. activity level was found to be 85 to 313 percent higher than the OECD average (varying by disease class). The report underscored that price controls would put this U.S. leadership position at risk. Depending on the therapeutic field, estimates show that price controls can result in a 50 percent or more reduction in early-phase research. Research on biologics and cancer could decrease by 59 and 54 percent, respectively, hampering life-sciences innovation and leading to fewer potentially life-saving therapeutics.[6]

The IRA's price controls distinguish between two types of drugs: small-molecule drugs, which are derived chemically, and biologics, which are derived from, and generally manufactured within, living tissues.[7] The IRA applies different timelines for when these two classes of drugs become eligible for price setting. It allows small molecules to be sold at market price for 9 years, and biologics for 13 years, before price setting begins.[8] (Small- and large-molecule drugs become subject to CMS "negotiations" after being on the market for 7 and 11 years, respectively.) The IRA implements this distinction through the use of two distinct drug approval processes: the New Drug Application (NDA), commonly used to review small molecule drugs, and the Biologics License Application (BLA), used for biologics.[9]

The IRA's arbitrary distinction between small-molecule and biologic drugs exerts a disproportionately negative effect on small-molecule drugs, which account for nearly 90 percent of all drugs on the market.[10]

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[5] Dana Goldman et al., "Regulating Drug Prices: U.S. Policy Alternatives in a Global Context" (RAND, 2008), https://www.rand.org/pubs/research_briefs/RB9412.html.

[6] U.S. Chamber of Commerce Global Innovation Policy Center, "From Innovation Oasis to Research Desert: The Impact of Price Controls on Clinical Research and Development," (U.S. Chamber of Commerce,2023), https://www.uschamber.com/assets/documents/From-Innovation-Oasis-to-Research-Desert-USCC.pdf

[7] Huy X. Ngo and Sylvie Garneau-Tsodikova, "What are the drugs of the future?" *MedChemComm* Vol. 9, No. 5 (2018): 757–758, https://pubs.rsc.org/en/content/articlelanding/2018/md/c8md90019a.

[8] Cubanski et al., "Explaining the Prescription Drug Provisions."

[9] Meena Seshamani, "Medicare drug price negotiation program: Revised guidance, implementation of sections 1191-1198 of the social security act for initial price applicability year 2026" (memorandum, Center for Medicare & Medicaid Services, June 30, 2023), https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf.

[10] F. D. Makurvet, "Biologics vs. small molecules: Drug costs and patient access" *Medicine in Drug Discovery* Vol. 9, 100075, https://www.sciencedirect.com/science/article/pii/S2590098620300622?via%3Dihub.

The IRA's impact on small-molecule drugs is especially pernicious because it cuts off the tail end of the revenue curve for these medicines. For instance, a study by RA Capital Management found that drug revenues from years 10 to 14 account for more than one-third of revenues and roughly 40 percent of the total net present value of a cardiovascular drug in the United States. Cutting off this important part of the revenue curve can make early-stage cardiovascular drugs not worth the investment.[11]

Ultimately, the IRA disincentivizes small-molecule development by shifting R&D incentives toward biologics. Yet neither type of drug is more important than the other. Both are needed to continue improving human health, and scientists should follow the science to determine which works best in treating a particular disease.[12] Importantly, small-molecule drugs can cross the blood-brain barrier, allowing them to treat a variety of diseases, ranging from allergies to neurodegenerative conditions, making them important for meeting the needs of underserved and elderly populations.[13] But as it stands, over the long term the IRA will only end up limiting patient access to a variety of affordable drug options, as fewer small-molecule drugs reach the market, decreasing accessibility for underserved and elderly populations, as small molecule drugs are cheaper to administer.

In August 2023, CMS released its initial list of the first 10 drugs to become subject to price setting, of which 7 were small-molecule drugs. In January 2025, CMS released a second list of the next 15 drugs to be subjected to price setting, with "negotiated" prices to take effect in 2027.[14] These drugs treat a wide range of disorders, from Type 2 diabetes to autoimmune disorders to cancer. All are small molecule drugs. Examples of the drugs include Xtandi, a treatment for nonmetastatic castration-sensitive prostate cancer; Otezla, a treatment for moderate to severe plaque psoriasis and psoriatic arthritis; and Tradjenta, a treatment for Type 2 diabetes.

Some contended that the effects of the IRA on U.S. biopharmaceutical innovation would be relatively benign. For instance, a 2022 Congressional Budget Office report found that the United States would lose just 15 potential drugs over the next 30 years due to lost revenues from drug price controls.[15]

Yet the actual reality is that the IRA has already exerted a profoundly deleterious impact on U.S. biopharmaceutical innovation activities (and will only continue to do so going forward). For instance, a report

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[11] Tess Cameron, Peter Kolchinsky, and Richard Xie in a presentation to economists: "Beyond total revenues… How the IRA impacts investors' early-stage R&D decision-making," November 11, 2023, RA Capital Management.

[12] Stephen Ezell, Leah Kann, and Sandra Barbosu, "The Inflation Reduction Act is Negotiating the United States Out of Drug Innovation," (ITIF, February 2025), https://itif.org/publications/2025/02/25/the-inflation-reduction-act-is-negotiating-the-united-states-out-of-drug-innovation/.

[13] Lindsey Seidlitz, "New resource underscores the importance of small molecule medicines," PhRMA, May, 4 2023, https://phrma.org/blog/new-resource-underscores-the-importance-of-small-molecule-medicines.

[14] CMS, "Medicare Drug Price Negotiation Program: Selected Drugs for Initial Price Applicability Year 2027," https://www.cms.gov/files/document/factsheet-medicare-negotiation-selected-drug-list-ipay-2027.pdf.

[15] Congressional Budget Office (CBO), "Estimated Budgetary Effects of Public Law 117-169, to Provide for Reconciliation Pursuant to Title II of S. Con. Res. 14," (CBO, August 2022), https://www.cbo.gov/publication/58455.

by Vital Transformation finds that small-molecule drug funding has dropped 70 percent since draft legislation that would become the IRA's drug pricing provisions was first tabled in September 2021.[16]

As the IRA pushes pharmaceutical companies and venture investors away from small-molecule medicine, over three-fourths of companies have said they are reconsidering their current strategies, shifting away from small-molecule drugs as they become economically unaffordable to pursue.[17] Fifty-seven percent of pharmaceutical companies interviewed by PhRMA reported they expect to reduce funding on projects that will take many years to develop.[18] As an example, in early 2024, Pfizer announced plans to alter its oncology treatment strategy toward more biologic drugs and to reduce small-molecule investment.[19] Elsewhere, Bristol Myers Squibb's CEO publicly announced that the company was conducting a thorough review of its portfolio, expecting to cancel certain programs in its effort to make financially sound decisions.[20] In total, 63 percent of PhRMA member companies report that they expect to shift R&D investment focus away from small-molecule medicines, meaning treatments for many common life-threatening diseases, including cancer, hypertension, and allergies, will likely see less innovation going forward.[21]

The IRA is also turning investors away from America's biopharmaceutical sector, which will inhibit the formation or growth of start-up companies that play such a key part of America's biopharmaceutical innovation system. Indeed, small pharmaceutical companies represent the source of more than 7 in 10 drug candidates currently in Phase III (pivotal stage) clinical trials.[22] Yet an informal survey conducted by Steve Potts, CEO of SLAM Biotherapeutics, found that out of 100 venture capital (VC) firms surveyed, over 75 percent are planning on divesting from small-molecule companies, as the return on investment in the wake of the IRA has become too unpredictable.[23] Potts noted that the shortened timeframe for small molecules indicates to VC firms that returns need to happen quicker in order for them to remain a good investment; but this trend has not been observed and is leaving investors wanting to turn away from the sector.[24]

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[16] Duane G. Schulthess et al., " The Inflation Reduction Act's Impact upon Early-stage Venture Capital Investments" (preprint, MedRxiv, January 7, 2025), https://doi.org/10.1101/2025.01.07.25320113.

[17.] PhRMA, "Inflation Reduction Act Already Impacting R&D," https://cdn.aglty.io/phrma/global/resources/import/pdfs/Infographic%20%20Inflation%20Reduction%20Act%20Already%20Impacting%20RD%20%20010923%20FINAL.pdf.

[18] Ibid.

[19] Greg Slabodkin, "IRA Drives Pfizer's Decision to Focus on Biologics, Not Small Molecules," *BioSpace*, March 4, 2024, https://www.biospace.com/ira-drives-pfizer-s-decision-to-focus-on-biologics-not-small-molecules.

[20] James Waldron, "Bristol Meyers CEO already reassessing portfolio in wake of US pricing law: report," *Fierce Biotech*, November 21, 2022, https://www.fiercebiotech.com/biotech/bristol-myers-already-reassessing-portfolio-wake-ira-ceo-tells-ft.

[21] PhRMA, "Inflation Reduction Act Already Impacting R&D."

[22] CBO, "Research and Development in the Pharmaceutical Industry" (CBO, April 2021), https://www.cbo.gov/system/files/2021-04/57025-Rx-RnD.pdf.

[23] Steve Potts, "The Future of Biotech," *Vital Health*, Podcast Audio, October 2024.

[24] Ibid.

PRICE SETTING DISCOURAGES CLINICAL TRIALS

IRA price controls also discourage post-approval trials, with potentially significant consequences for oncology and other therapeutic areas where pursuing additional indications or patient populations after initial approval is crucial to tackling unmet medical needs. Overall, the IRA is likely to decrease incentives for such post-approval trials by setting a limited timeframe before a drug becomes eligible for price setting, regardless of other indications.[25]

Post-approval trials, which can lead to novel drug indications or formulations, require significant investment in R&D, as they are not simply adjacent knowledge. An analysis by ATI Advisory—a health-care research and advisory services firm—of the R&D costs for the first 10 Medicare Part D drugs selected for price setting under the IRA finds that, on average, 61 percent of R&D costs are incurred after a drug's first FDA approval. For six out of the eight drugs with data on clinical trial starts, most trials—ranging from 54 to 84 percent—started after approval, highlighting the importance of post-approval R&D to advancing medical knowledge.[26]

It should also be noted that, by compromising drug innovation today, the IRA compromises generic drug availability tomorrow. Generic and biosimilar drugs have played vial roles in helping manage drug prices for U.S. citizens. In 2023 alone, generic and biosimilar prescription medicines saved $445 billion for the U.S. healthcare system overall, while they have saved more than $3.1 trillion saved over the past 10 years.[27] But an innovative drug that's never made today becomes a generic drug that never makes it to market tomorrow.

CONCLUSION

In February 2025, Representatives Greg Murphy (R-NC), Don Davis (D-NC), and Richard Hudson (R-NC) reintroduced the Ensuring Pathways to Innovative Cures (EPIC) Act in Congress. The legislation seeks to limit to some degree the damage inflicted by the IRA on America's biopharmaceutical innovation system. Specifically, the EPIC Act would give small-molecule drugs the same market time before price setting as biologics get, allowing both drugs 13 years on the market before becoming subject to government price setting.[28]

The biopharmaceutical industry is crucial to the U.S. economy. America is the global leader in this sector thanks to its large domestic market, robust IP protections, historically limited government drug price setting, supportive science policies, and innovative regional biotech clusters. But recent policies permitting CMS price

[25] Stacie B. Dusetzina and Frank S. David, "Cancer Drug Access and Innovation Under the Inflation Reduction Act—A Balancing Act" *JAMA Oncology* (October 24, 2024), https://doi.org/10.1001/jamaoncol.2024.4745.

[26] ATI Advisory, "First 10 Drugs Selected for Medicare Negotiation," (ATI Advisory, 2023), https://atiadvisory.com/resources/first-10-drugs-selected-for-medicare-negotiation/.

[27] Association for Accessible Medicines, "Generic and Biosimilar Medicines Save $445 Billion in 2023," news release, September 5, 2024, https://accessiblemeds.org/resources/press-releases/generic-and-biosimilar-medicines-save-445-billion/.

[28] Congress.gov, "H.R.1492," https://www.congress.gov/bill/119th-congress/house-bill/1492.

setting are hamstringing the industry, as they reduce incentives for pharmaceutical companies to invest in future drug R&D to create life-improving and life-saving medicines.[29]

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[29] Sandra Barbosu, "Not Again: Why the United States Can't Afford to Lose Its Biopharma Industry," (ITIF, February 2024) https://itif.org/publications/2024/02/29/not-again-why-united-states-cant-afford-to-lose-biopharma-industry/.