Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

Biotechnology Innovation Organization
Statement for the Record
U.S. House Committee on Ways & Means Subcommittee on Health
Examining Policies that Inhibit Innovation and Patient Access
May 10, 2023

The Biotechnology Innovation Organization (BIO) appreciates this opportunity to present these comments to the Committee as it examines policies that will have negative effects on medical innovation and reduce patient access to therapies. Our comments focus on two areas that threat patient access to innovative medicines in Medicare: (1) the anti-innovation policies enacted as part of the Inflation Reduction Act (IRA) (2) government policies that that are blocking patient access to new FDA-approved treatments.

BIO is the world's largest trade association representing nearly 1,000 biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, delay the onset of such diseases, or prevent them in the first place. As a result, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes but also have reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

IRA Impacts and Recommended Actions

The IRA authorizes the Secretary of Health and Human Services to "negotiate" the price Medicare pays for certain medicines. With stiff penalties for companies that don't comply, these are not so much negotiations but more aptly named, "price controls". These price caps will be imposed on 100 medicines in the Medicare program by 2031. These government price controls will hurt innovators – particularly small biotech – and patients desperate for new treatments.

New medicines are extremely costly to develop, requiring enormous amounts of private investment – but the IRA threatens these investments. Health consulting firm Avalere estimates that the IRA will cost biotech companies $450 billion over the next decade. Such a staggering reduction in revenue will obviously lead to cuts in R&D spending. According to estimates by University of Chicago economist Tomas J. Philipson, the IRA's price controls could result in 135 fewer new drug approvals for patients and the consequent loss of 331 million life years by 2039.

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

Certain areas of research will feel the impact more than others because the IRA's price controls apply differently to different kinds of medicine. So-called "small molecule" drugs are subject to price controls just nine years after earning FDA approval. By contrast, biologics – complex medicines derived from natural sources – are subject to price controls after 13 years. Most pharmaceuticals on the market today, including, for example, 89 anti-tumor drugs for treating cancer, are small molecule. But the IRA disincentivizes and penalizes this critical research and robs patients of life-changing new treatments. Further research on oncology medicines continues after FDA approval. That's when scientists perform additional tests to determine whether a medicine developed to treat one cancer is effective at treating another. But the threat of near-term price controls makes companies much less likely to invest in additional post-approval research.

We're already seeing companies move away from small-molecule research. For instance, Eli Lilly said it would stop work on a small-molecule treatment for blood cancer that was already in clinical trials.[1] Novartis and GSK have also cancelled or suspended cancer-drug projects.[2] Cancer isn't the only research area that will suffer. For example, for neurological diseases like Alzheimer's, small-molecule medicines offer some of our best prospects for breakthroughs. Meanwhile, Alnylam recently ended plans to test its drug Amvuttra to treat the rare Stargardt eye disease, citing the potential impact of the IRA.[3]

This unfortunate trend is likely to worsen as long as IRA price controls remain in place. To address it, Congress should repeal this price control mechanism. Absent repeal, critical steps should be taken to help mitigate the IRA's damaging effects. An important first step would be to apply the same 13-year window to both small-molecule drugs and biologics.

Other steps should be taken as well. The orphan drug exemption from price controls is too limited and will stifle research and development into rare and hard-to-treat diseases. Specifically, orphan drugs designated for *only one* disease or condition and approved for only that one disease or condition are exempt from negotiation. Any subsequent designations – even for another orphan condition – would result in the elimination of the exemption for all orphan conditions. This exemption should be modified to allow for multiple orphan indications to be exempt from price controls. According to IQVIA, of the 564 drugs

[1] https://www.reuters.com/business/healthcare-pharmaceuticals/drug-companies-favor-biotech-meds-over-pills-citing-new-us-law-2023-01-13/

[2] https://endpts.com/eli-lilly-rolls-snake-eyes-as-it-axes-two-early-stage-drugs-including-a-40m-cancer-therapy-from-fosun/#:~:text=Senior%20Editor,a%20%2440%20million%20cancer%20drug.

[3] https://www.bloomberg.com/news/articles/2022-10-27/alnylam-halts-work-on-eye-drug--citing-new-us-law-over-pricing

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

with orphan approvals, 104 of these drugs are approved for two or more indications – most of which are for rare cancers and blood disorders.[4]

In addition, the time-limited exemption from price controls for small biotech drugs – which currently expires in 2029 – should be made permanent. Biotech companies generally focus on early- and mid-stage research, and they typically lack the resources to conduct late-stage, hugely expensive clinical trials or build out a worldwide sales and distribution network. That's why they often partner with larger companies that have more production and distribution experience. Vital Transformations recently analyzed a cohort of 363 new medicines approved by the FDA between 2011 and 2020 and found that 55 percent were developed by small firms with less than $500 million in annual revenue. But it was large companies who managed post-FDA approval development, marketing, and scale for many of these medicines. The success of this diversified ecosystem has led to a 152 percent increase in U.S. external R&D partnerships and investments since 2011, per Vital Transformations estimates.

CMS Implementation – Recommended Improvements

Congress should also increase its oversight of the Centers for Medicare & Medicaid Services (CMS) as the Agency moves forward in implementing the IRA's price negotiation program. It is critical that CMS implement this program in a fair, predictable, and transparent manner with the ultimate goal of maintaining patient access to all necessary therapies.

To that end, we note our strong disappointment that key aspects of CMS' draft initial guidance were issued as final without allowing for comments from stakeholders, which is a concerning step backward from CMS's stated commitment to transparency. The need for such a fulsome process is especially acute here, given the novelty and complexity of the Negotiation Program; the vast ramifications that the program will have for patients, providers, pharmacies, manufacturers, and countless other stakeholders; and the potentially profound negative repercussions for patient access to needed therapies that could follow from errors, misunderstandings, or gaps in understanding. In these circumstances, the Agency should maximize transparency and engagement in its decision-making process, including by both affording a full opportunity for comment and meaningfully responding to stakeholder feedback.

A critical policy that CMS finalized without opportunity for comment was its decision that, in determining which drugs are eligible for negotiation, it would not treat drugs approved under unique New Drug Applications (NDAs) or Biologics License Applications (BLAs) as distinct drugs but, rather, would combine NDAs and BLAs with the same active

[4] See: https://www.iqvia.com/insights/the-iqvia-institute/reports/orphan-drugs-in-the-united-states-rare-disease-innovation-and-cost-trends-through-2019

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

moiety/active ingredient together for negotiation purposes. CMS must reverse this policy as it is bad for innovation, bad for patients, and not supported by the statute. CMS's approach leaves no incentive for therapeutic advancement and will have significant, negative impacts on innovation for years to come. Biopharmaceutical innovation is incremental, relying on sustained and continuous improvements to molecules, pathways, and modes of administration to achieve maximum clinical benefit for patients. Researchers cannot take significant leaps and develop new active moieties with each generation of treatment. By combining drugs at the active moiety or active ingredient level, CMS is harming investments into new therapies, including for orphan and hard to treat diseases. For the sake of pharmaceutical and biotechnology innovation, and patient access to needed therapies, CMS's current framework cannot stand.

CMS also needs to take a number of steps to ensure that its negotiation process is fair, predictable, and transparent. The statute mandates that CMS "develop and use a consistent methodology and process" for MFP negotiation. Although no two negotiations will ever be identical—because the circumstances of each selected drug are unique—all negotiations should be subject to a clear and reasonable framework. A consistent process not only is statutorily required but also helps to ensure that CMS complies with its obligation to treat similarly situated entities in a similar manner, absent a reasoned basis for distinction. CMS's proposed process falls far short of these principles.

We recommend a number of actions CMS should take to enable a negotiation process that allows for meaningful engagement and dialogue between CMS and manufacturers, including providing for in-person meetings throughout the process. Manufacturers should also be permitted to supplement initial submissions to CMS. Permitting supplemental submissions is well warranted. Under the statute, manufacturers are given only one month to prepare a voluminous submission of complex information, including information regarding Non-Federal average manufacturer price (non-FAMP); research and development costs; production and distribution costs; federal financial support for discovery and development; pending and approved patent applications, FDA exclusivities, NDAs or BLAs and approvals thereof, market data; and revenue and sales volume data. In some cases, requested data may also not exist in a format required by CMS, such that the manufacturer will need to painstakingly convert raw data from multiple sources into such a format. Manufacturers will assuredly work with utmost diligence to comply with CMS's submission requirements. Still, they may need the flexibility of a supplement to their timely submission for legitimate reasons.

In addition, CMS should provide a meaningful justification of its initial offer to a manufacturer, as well as any response to a manufacturer's counteroffer and afford the manufacturer a meaningful opportunity to comment on the response the MFP is set. As with any good faith negotiation, open dialogue will be vital to the success of the MFP negotiation. To this end, CMS should specify that its initial offers and its responses to any counteroffers include meaningful explanations of how the Agency arrived at the offer or response,

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

including how the offer or response is supported by the statutorily enumerated negotiation factors and any other information upon which the Agency relied, and how the Agency considered and weighted such factors and information.

CMS must also clarify how its review of the evidence will inform its setting of the MFP. CMS's approach remains unclear and presents untenable levels of uncertainty. Essentially, CMS has said it will use the net price of the "therapeutic alternatives" of drugs selected for negotiation as a starting point and then adjust this starting point based on its review of the clinical evidence. In addition, CMS has said it may make further adjustments based on other data manufacturers are required to submit, such as "recoupment" of research and development costs. But CMS has not provided a framework for how it will review all this evidence. Nor has the agency indicated how certain evidence or factors will be weighed. This lack of clarity and uncertainty is of great concern and our position is that CMS should clarify its standards for evidence review and be transparent and accountable about what evidence drove its decisions in setting the MFP and why. Further, CMS's review of the evidence should focus on factors that are critical for patients, specifically factors related to clinical benefit and unmet medical need and de-emphasize manufacturer specific data elements such as cost of production and research and development costs.

Finally, CMS should eliminate its proposed, one-sided requirement that manufacturers destroy all records related to the negotiation process and submit a Certificate of Data Destruction to CMS certifying that all information received from CMS during the negotiation period and potential renegotiation period(s) was destroyed. Basic due process mandates that manufacturers be given the ability to maintain records related to negotiation proceedings. Moreover, BIO opposes the blanket prohibition on manufacturers from disclosing or otherwise publicizing information "in the initial offer, including the ceiling price, or the concise justification from the Secretary or any subsequent offer of concise justification, nor information derived from those justifications or offers…". This one-sided information control heightens the ultimate public complaint that the entirety of the "negotiation" process is anything but actual "negotiation." BIO disagrees with this approach – which essentially allows CMS to operate in secret with no accountability – and recommends CMS abandon it.

What is more, CMS appears to be making a more general affront to the protected speech of affected manufacturers. As has been reaffirmed many times before, prior restraints on speech are presumptively unconstitutional.[5] The government faces a heavy burden in showing a compelling interest in keeping negotiation discussions private, and we fail to see a legitimate reason why the government's interests are so advanced by muzzling private

[5] *See, e.g., Near* v. *Minnesota* 283 U.S. 697 (1931).

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

companies in the context of Medicare price negotiation discussions.[6] In fact, in this instance, any potential disclosure by a manufacturer would likely relate to truthful information that is, at a minimum, of significance to at least a portion of the public involved in the transaction of health insurance and health consumption. As such, we recommend CMS abandon these burdensome and unnecessary confidentiality and anti-disclosure provisions.

Government Action that Harms Access: Limiting Coverage for Drugs Approved under FDA's Accelerated Approval Pathway

Originally conceived to address one of the world's most daunting public health challenges—the AIDS epidemic—and reinforced for use in cancer and rare diseases, the FDA's accelerated approval pathway has yielded more than 270 treatments over its 30 years.[7] These treatments give patients with life-threatening diseases therapeutic options where minimal or none previously existed. Yet, this approval pathway has come under attack by both public and private payers, claiming accelerated approval drugs are improperly driving spending and questioning the FDA's approval decisions.

Under the accelerated approval pathway, the FDA may approve a drug intended to ameliorate serious unmet medical need that demonstrates safety and efficacy in well-controlled clinical trials where efficacy is based on a surrogate or an intermediate clinical endpoint that is reasonably likely to predict clinical benefit, rather than the primary clinical outcome that may take years to measurably manifest.

Yet, critics of the pathway mistakenly claim that accelerated approval drugs do not meet the FDA's "full" standard for safety and efficacy. These concerns are the basis for current policy proposals proposed by several state Medicaid programs, the Medicaid and CHIP Payment and Access Commission (MACPAC) and recent comments by the Medicare payment Advisory Commission (MedPAC) These off-base pronouncements come, even as the FDA has been clear that approval through its accelerated approval program is no half measure or anything less than "full" approval.[8]

---

[6] As has been reaffirmed in many instances by the US Supreme Court, the government must articulate a compelling government need for the negotiation to remain out of the public discourse and must simultaneously introduce a narrowly tailored method for so restricting this discussion. In the context of this guidance, we see no such articulation of either a compelling need nor a narrow restriction. In fact, we see just the opposite. *See, e.g., New York Times Co.* v. *United States,* 403 U.S. 713 (1971).

[7] Kenneth E. Thorpe and Thomas L. Johnson, "Accelerated Approval Drugs Are Not Driving Medicaid Spending" Health Affairs, June 3, 2022.

[8] FDA, "Accelerated Approval Program," Last Updated January 30, 2023. Accessed May 5, 2023. https://www.fda.gov/drugs/nda-and-bla-approvals/accelerated-approval-program#:~:text=The%20FDA%20instituted%20its%20Accelerated,based%20on%20a%20surrogate%20endpoint.

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

To further illustrate the gravity of the issue, CMS recently announced the decision that Medicare would cover monoclonal antibodies targeting amyloid plaque for the treatment of Alzheimer's only if they have received traditional (i.e., not accelerated) approval from the U.S. Food and Drug Administration (FDA); drugs receiving Accelerated Approval would only be covered for patients in clinical trials. This decision, as we described at the time, was an "enormous setback for Alzheimer's patients and an unprecedented and dangerous infringement on the FDA's scientific autonomy and decision making." This dangerous precedent of CMS substituting its own judgement for FDA's could lead to a dangerous spiral of lack of confidence in the U'S''s gold standard drug approval process, access restrictions or continued unmet need for patients suffering from all manner of diseases and ailments, and a disinvestment of an important industry where our country is far and away the global leader.

Still more troubling for patients suffering with unmet medical need is that CMS's Alzheimer's decision is neither isolated nor unique among policymakers. A recent proposal was floated by the Center for Medicare and Medicaid Innovation (CMMI), to reduce Medicare spending on drugs entering the market via accelerated approval, if confirmatory phase 4 trials are not complete. This troubling approach has the potential to decrease patient access to drugs for serious conditions with unmet needs. Specifically, for investigational products, the proposal would disincentivize future product development and investment. Additionally, for products that are currently approved under the accelerated approval pathway, the program may discourage sponsors from pursuing the required post-approval studies and maintaining the product approval in the United States. The healthcare consultancy Vital Transformation has found that threats such as these at both the federal and state level could result in as many as two-thirds of accelerated approval therapies failing to reach patients – affecting as many as 3.6 million patients.[9]

BIO strongly opposes efforts to restrict access to innovative therapies approved under the accelerated approval pathway. This pathway is often the only mechanism for approving effective therapies to address critical unmet patient need in challenging and serious disease states. Any efforts to undermine this pathway would have serious, detrimental effects on vulnerable patient populations and hinder innovation.

Critics miss that using the same well-established evidentiary standard as for traditional approvals, the pathway has facilitated approval of treatments for many severe diseases, such as a variety of cancers (including rare cancers), Human Immunodeficiency Virus (HIV), various bacterial infections, Multiple Sclerosis, Sickle Cell Disease, and others. Moreover, drugs earning accelerated approval must meet the same statutory standards of evidence for safety and effectiveness as those granted traditional approval. In using the accelerated

[9] https://vitaltransformation.com/2022/06/calculating-the-value-and-impact-of-accelerated-approvals/

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

approval pathway, a sponsor must show that the drug demonstrates substantial evidence of an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict a clinical benefit.

Further, drug manufacturers are required to conduct with due diligence phase 4 post-marketing trials to verify the clinical benefit of the drug. FDA may withdraw the accelerated approval if evidence demonstrates that the product is not shown to be safe or effective. This happens if the post-marketing trials do not verify clinical benefit or are not conducted with due diligence.

For all these reasons, we urge the Committee to oppose efforts to restrict access to innovative therapies approved under the accelerated approval pathway, which is often the only way forward for approving effective therapies to address critical unmet patient need.

Government Action that Harms Access: The Need to Limit CMMI Authority

BIO believes that innovation is key to bringing cures and treatments to patients suffering from unmet medical need. To that end, we believe innovation in existing payment systems may be just as critical as innovation in the laboratory to deliver tomorrow's cures. Today's 20th Century payment systems often have difficulty delivering 21st Century treatments that do not fit neatly into decades-old legacy payment systems. Concomitantly, we support CMMI's goal to "foster healthcare transformation."

At the same time, BIO believes that great amount of authority invested in CMMI must be wielded to truly innovate the American health care system rather than to facilitate an end run around the Congress' authority to oversee the Medicare program. As illustrated above in its recent approach to cutting spending on drugs approved through the accelerated pathway, CMMI's broad testing authority, and CMS's increasingly aggressive approach to using that authority, results in unchecked ability of the Agency to make rapid, broad, and unpredictable changes to payment policy. Several recent CMMI announcements (Radiation Oncology Model, International Pricing Index Model, and past mandatory demonstrations such as the Part B Drug Payment Model and Comprehensive Care for Joint Replacement Model), illustrate the negative consequences such action can have for patients, providers, and other stakeholders. Reforms are urgently needed to establish CMMI safeguards so the agency can still propose and test new payment models, but protect against sweeping, unilateral policy changes that undermine care quality and patient access to needed care.

BIO has long supported bipartisan Congressional efforts to establish transparency and important guardrails around CMMI demonstration initiatives. These necessary CMMI reforms fall into five broad categories:

Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

(1) **Limiting mandatory Phase I tests:** Mandatory models pose heightened risks for negative, unintended consequences for patient care, care quality, and care continuity. Phase I models should be tested on a voluntary basis to minimize and assess the potential risks to beneficiaries.

(2) **Placing reasonable limits on the scope and duration of CMMI models:** Set appropriate limits on the number of beneficiaries that can be included in any early-stage test (the lesser of either 10% of the defined population or 500,000 beneficiaries) and limit the length of time the demonstration can run to no more than 5 years.

(3) **Reaffirming the need for Congressional approval of any legislative changes required to expand a model**: Under the statute, CMMI may waive certain provisions of law in order to test models but may not make permanent changes to the law. To reaffirm Congress' role in making changes to Medicare law, legislation should clarify that Congress must approve any changes to existing statute (if needed) when CMMI expands a model (Phase II).

(4) **Providing for judicial review of key CMMI decisions:** Current CMMI statute precludes key mechanisms for accountability at CMMI by limiting judicial review of CMMI decisions. Reforms are needed to allow for judicial review and promote CMMI accountability for important decisions (e.g., regarding model expansions).

(5) **Improving accountability and stakeholder engagement and establishing stronger safeguards for beneficiaries:** CMMI models should be developed with input from impacted stakeholders prior to their announcement through a request for applications or proposed rule. Stronger safeguards are also needed at model launch to protect beneficiaries, including a monitoring and evaluation strategy appropriate to the risks associated with the model and providing for notification to impacted beneficiaries.

Conclusion

We thank the Subcommittee for the opportunity to provide this statement for the record for the hearing, "*Examining Policies that Inhibit Innovation and Patient Access.*" We look forward to working with the Committee to address these important issues and stand ready to help the Subcommittee in any way we can to assure access to new cures and treatments for Americans suffering from diseases of all kinds.