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VIA ELECTRONIC FILING TO: www.regulations.gov

February 23, 2026

The Honorable Mehmet Oz, MD
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1832-P
P.O. Box 8016
Baltimore, MD 21244-8016

Re: Guarding U.S. Medicare Against Rising Drug Costs (GUARD) Model (CMS-5546-P)

The Biotechnology Innovation Organization (BIO) appreciates the opportunity to comment on the Center for Medicare and Medicaid Services' (CMS's/the Agency's) Guarding U.S. Medicare Against Rising Drug Costs (GUARD) Model (CMS-5546-P) proposed rule (Proposed Rule).[1]

BIO is the premier biotechnology advocacy organization representing biotech companies, industry leaders, and state biotech associations in the United States and more than 35 countries around the globe. BIO members range from biotech startups to some of the world's largest biopharmaceutical companies—all united by the same goal: to develop medical and scientific breakthroughs that prevent and fight disease, restore health, and improve patients' lives.

BIO strongly opposes GUARD and urges the Administration to withdraw the Proposed Rule in its entirety. We look forward to working with the Agency on alternative policies that address global free-riding and promote patient access. Our detailed comments on the Proposed Rule are presented below. We thank CMS for its consideration of our comments.

[1]Guarding U.S. Medicare Against Rising Drug Costs (GUARD) Model, 90 Fed. Reg. 60,338 (Dec. 23, 2025) (proposed to be codified at 42 C.F.R. pt. 514).

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I. Overview

BIO strongly opposes GUARD and urges the Administration to withdraw the Proposed Rule in its entirety. While BIO supports the underlying policy aims of reducing foreign free-riding and improving patient outcomes by reducing their out-of-pocket costs, this illegal GUARD "model" would be profoundly harmful to American patients and cause irreparable harm to U.S. biotechnology investment. GUARD would implement government price controls in Medicare, allowing foreign nations and non-U.S. companies to dictate pricing policies for U.S. pharmaceutical manufacturers, and bring to the U.S. all of the well-known negative consequences that such pricing policies have had in other nations: reduced incentives for innovation and slower, narrower access to new treatments.[2]

In so doing, GUARD violates numerous statutory boundaries on the authority of the Center for Medicare and Medicaid Innovation (CMMI)—attempting to rewrite CMS's statutory authority, which is restricted to genuine, limited tests of payment and service delivery innovations, in order to invent a new mandatory, nationwide, punitive price-setting framework based on activities that take place entirely outside the U.S. The proposal also violates numerous core constitutional and legal principles, including "major questions" doctrine, appropriations law, principles of the Presentment, Due Process, and Takings clauses, separation of powers and non-delegation doctrine, and Congress's enumerated powers over foreign commerce and patents. GUARD also raises serious administrative law and procedural concerns, including inadequate consideration of key issues that would lead to arbitrary and capricious policy, and the inability for stakeholders to provide meaningful comment given the proposal's significant uncertainty and unpredictability.

Beyond these serious legal defects, GUARD does not help patients with the access concerns that directly impact and matter to them, namely, harsh benefit management policies (e.g., prior authorization, step therapy, and restrictive formulary schemes) and high plan cost-sharing requirements that interfere with patient access. For patients who need ongoing access to essential medications recognized by Congress through the "six protected class" (6PC) policy—drugs specifically targeted by GUARD—these harmful policies are especially prevalent and particularly harmful.[3] Instead, CMS professes concern for out-of-pocket costs that have been meaningfully addressed by recent reforms. And in fact, CMS anticipates that GUARD could indirectly lead to increased rather than decreased out-of-pocket costs for seniors on Medicare.[4]

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[2] *See e.g.*, CONG. BUDGET OFF., *Re: Effects of Drug Price Negotiation Stemming from Title I of H.R. 3*, (Oct. 11, 2019), https://www.cbo.gov/system/files/2019-10/hr3ltr.pdf; Carmelo Giaccotto, Rexford E. Santerre & John A. Vernon, *Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry*, 48 J. L. & ECON. 1 (2005); *Proliferation of Innovation Over Time: Frequency, Timing and Clinical Value of Expansions Post-Initial Approval*, IQVIA INSTITUTE FOR HUMAN DATA SCIENCE (Feb. 18, 2025), https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/proliferation-of-innovation-over-time.

[3] *Medicare Part D's Six Protected Classes Policy: Coverage Policies Create Access Challenges for Patients with Complex Chronic Conditions*, P'SHIP FOR PART D ACCESS (Feb. 2021), https://www.partdpartnership.org/uploads/8/4/2/1/8421729/avalere_report_on_six_protected_classes_--_february_2021.pdf.

[4] *See* 90 Fed. Reg. 60,340, 60,348.

Meanwhile, voluminous evidence has shown that international reference pricing policies, including the pricing policies of those countries GUARD would rely on, have resulted in reduced investment in biotech research and development and slower introduction of new therapies.[5]

Layering such policies on top of the Inflation Reduction Act's (IRA's) price-setting provisions will compound the damage that federal policy has already recently done to incentives for biotechnology investment. International reference pricing risks ending the U.S.'s global leadership in biotechnology, at a time when such leadership is already under real threat from China and other foreign competitors. GUARD's approach will also be especially damaging to the uniquely dynamic American ecosystem of small- and medium-size firms that serve as the discovery engine for new medicines, including medicines to treat rare diseases. These companies are particularly sensitive to expected returns and policy uncertainty and cannot weather the policies mandated by GUARD, forcing them to face a host of terrible choices.

Most important, patient access is at stake. Experience in many European systems shows that aggressive price controls can be accompanied by delayed launches or decisions not to launch at all.[6] Mandating rigid international benchmarks in these areas risks forfeiting the kinds of breakthroughs patients are waiting for. This dynamic is especially problematic for rare disease therapies and complex therapies, where small patient populations, high development costs, and complex manufacturing already make investments in such areas especially risky, and arbitrary international pricing will substantially increase these risks.

We address each of these concerns in greater detail, below.

BIO also stands ready to work constructively with the Administration on policies that are focused on improving affordability and access at the point of sale and correcting distortions in the U.S. health care system without sacrificing future treatments and cures. This includes, for instance, building on recently passed pharmacy benefit management reforms to redirect the billions of dollars that currently line the pockets of middlemen to instead reduce patient out-of-pocket costs, and to ensure the billions of dollars in discounts manufacturers offer under the 340B program translate to lower out-of-pocket costs for patients—the program's true intended beneficiaries. On an international level, the Administration should continue to push for pricing policies that provide appropriate incentives for biotech innovation, including by brokering trade deals under which foreign countries start to pay their fair share for this progress. Such policies would help fulfill the Trump Administration's goals of supporting American innovation, improving patient access, and improving Americans' health. Importing failed pricing policies from other countries would deliver the exact opposite.

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[5] *See e.g.*, Ganeswar Matcha, *The Global Risks of America's "Most-Favored-Nation" Drug Pricing Policy,* THE PETRIE-FLOM CTR. (May 22, 2025), https://petrieflom.law.harvard.edu/2025/05/22/the-global-risks-of-americas-most-favored-nation-drug-pricing-policy/.

[6] *See e.g.*, Andrew W. Mulcahy et al., *Comparing New Prescription Drug Availability and Launch Timing in the United States and Other OECD Countries*, RAND CORP. (2024), https://www.rand.org/pubs/research_reports/RRA788-4.html.

II. GUARD Exceeds CMMI's Authority Under Section 1115A

CMS purports to establish GUARD pursuant to its authority under Section 1115A of the Social Security Act.[7] However, as explained herein, GUARD exceeds the specific limits Congress placed on the agency under this provision.

Section 1115A authorizes CMS, through CMMI, to test "innovative payment and service delivery models" expected to reduce program expenditures under Medicare, Medicaid, and the Children's Health Insurance Program (CHIP) while preserving or enhancing quality of care for the beneficiaries of these programs.[8] While CMS has certain discretion in selecting models for testing, this discretion is limited to those models where CMS "determines that there is evidence that the model addresses a defined population for which there are deficits in care leading to poor clinical outcomes or potentially avoidable expenditures." Moreover, CMS must "focus on models expected to reduce program costs under the applicable title while preserving or enhancing the quality of care received by individuals receiving benefits under such title."[9] CMS also must test such models using a phased approach, beginning with a more limited "Phase I" test before CMS can move to a broader "Phase II." CMS is further required to evaluate each model test including "an analysis of the quality of care furnished under the model, which includes the measurement of patient-level outcomes and patient-centeredness criteria" and the "changes in spending under the applicable titles by reason of the model."[10] While CMS is granted the authority to waive statutory requirements of the Medicare program, such waivers must be "necessary solely for purposes of . . . testing models."[11]

GUARD does not satisfy any of these requirements and instead represents an unlawful attempt to unilaterally amend the Medicare statute in a manner inconsistent with policy preferences expressly established by Congress.

A. GUARD is Not a True "Test."

Section 1115A directs CMS to *test* Phase I models to determine their effects on program spending and quality of care for beneficiaries.[12] The ordinary meaning of that term and the overall statutory design presuppose a limited experiment: a Phase I model must have an identifiable "research or experimental goal" that is "likely to yield useful information or demonstrate a novel approach to program administration."[13] However, CMS does not articulate any credible way in which GUARD functions as an experiment to observe whether expenditures rise or fall, or whether there is a change in beneficiary outcomes. Rather, CMS simply imposes a punitive manufacturer rebate scheme that guarantees program savings and then passively

[7] 42 U.S.C. § 1315a; 90 Fed. Reg. 60,338.
[8] 42 U.S.C. § 1315a(a)(1).
[9] *Id.* § 1315a(b)(2)(A).
[10] *Id.* § 1315a(b)(4).
[11] *Id.* § 1315a(d)(1).
[12] 42 U.S.C. § 1315a(b)(1).
[13] *See Beno v. Shalala*, 30 F.3d 1057, 1069 (9th Cir. 1994); *Test*, MERRIAM-WEBSTER DICTIONARY, https://www.merriam-webster.com/dictionary/test (last visited Feb. 16, 2025).

collects the resulting proceeds.[14] An initiative that merely and predictably offsets a portion of government spending through rebates is not a model test.

Leaving aside the obvious decrease in program spending that would result from CMS's collection of additional rebates from manufacturers, which does not in itself test anything at all, GUARD has at best a tenuous connection to any provider or patient behavior that could be tested. Meanwhile, any effects of GUARD on program spending or quality would be intertwined with other market forces stemming from other recent drug pricing and payment initiatives enacted by Congress, as well as other CMMI initiatives. Most notably, GUARD would interact with the GENErating cost Reductions fOr U.S. Medicaid (GENEROUS) Model, which also involves international reference pricing.[15] To the extent GUARD would have meaningful effects to reduce program spending—beyond the obvious impact of the government's collection of additional rebates from manufacturers—it would be virtually impossible to isolate and evaluate them as the statute requires.

That GUARD is not a test is underscored by the agency's failure to delineate any clear policy to address these overlaps. In the Proposed Rule, CMS states that "[i]f certain manufacturers were excluded due to interactions with other CMS Innovation Center models or for any other reason, the impacts from this proposed demonstration could be significantly less than described in this analysis."[16] This indeterminacy further highlights the absence of any model test theory and calls into question whether CMS could evaluate the impact of GUARD at all.

Instead, the one discernible outcome of GUARD on program spending—the collection of rebates by CMS, which in some cases may exceed the purchase price of the drug,[17] is effectively predetermined and arguably punitive.

B. GUARD is Not an Innovative "Payment and Service Delivery" Model.

Section 1115A limits the scope of CMS's authority to the testing of innovative "payment and service delivery models."[18] The phrase "payment and service delivery model" plainly describes a singular directive for model tests to address both payment and service delivery. This reading is reinforced by Congress's own examples of model test opportunities enumerated in section 1115A(b)(2)(B), each of which is specific to care delivery.[19] To the extent the examples involve payment, each pairs payment adjustments with delivery-related conduct such as promoting primary care payment and practice reforms that transition practices from fee-for-

[14] *See* 90 Fed. Reg. 60,347.
[15] CMS, *GENEROUS Model*, https://www.cms.gov/priorities/innovation/innovation-models/generous (last visited Feb. 6, 2026).
[16] 90 Fed. Reg. 60,409.
[17] This can occur if the price the U.S. purchaser pays for the drug is less than the spread between the benchmark and Medicare payment rate.
[18] 42 U.S.C. § 1315a(a).
[19] *See, e.g.*, 42 U.S.C. § 1315a(b)(2)(B)(xvi) ("Facilitate inpatient care, including intensive care, of hospitalized applicable individuals at their local hospital through the use of electronic monitoring by specialists, including intensivists and critical care specialists, based at integrated health systems.").

service toward comprehensive payment, risk-based contracting with groups of health care providers to promote innovative care delivery, or varying physician payment based on adherence to appropriateness criteria for ordering imaging services.[20] These illustrations confirm that Congress intended to authorize only those model tests that link payment changes to how care is actually provided.[21]

GUARD substantially departs from the structure of model tests authorized under section 1115A, in that it alters only the amount of rebates paid by manufacturers to CMS for Model drugs.[22] GUARD does not modify how any Medicare services are furnished, coordinated, or delivered to beneficiaries.[23] It does not even alter how the drugs are paid for by Part D plans or by beneficiaries. As such there is no colorable argument that GUARD will alter care delivery, even indirectly through changes in payment structure. In short, GUARD is wholly unconnected to service delivery while having an indeterminate relationship to patient out-of-pocket payments for their drugs.[24]

In sum, rather than testing innovative "payment and service delivery," the obvious and direct subject of the proposed Model is the imposition of additional rebates, and the obvious and direct beneficiary is the federal government's Medicare trust funds.[25]

It is also worth noting that GUARD is not innovative. Throughout the preamble to the GUARD proposal, CMS uses the word "innovative" multiple times (e.g., referring to the model as an "innovative payment model" that includes an "innovative alternative rebate calculation"). Yet GUARD is merely charging a new rebate in order to draw more dollars into the Medicare Trust Funds, and charging manufacturers rebates is hardly innovative.

As such, GUARD is clearly beyond the bounds of authority for CMS to engage in model tests under section 1115A.

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[20] *Id.* § 1315a(b)(2)(B)(vi).

[21] *Id; see also id.* (For example, models outlined in statute include "[p]romoting care coordination between providers of services and suppliers that transition health care providers away from fee-for-service based reimbursement and toward salary-based payment" and [v]arying payment to physicians who order advanced diagnostic imaging services . . . according to the physician's adherence to appropriateness criteria for the ordering of such services, as determined in consultation with physician specialty groups and other relevant stakeholders."

[22] 90 Fed. Reg. at 60,352 (acknowledging that "the GUARD Model does not directly impact Part D enrollee's out-of-pocket costs for these drugs.")

[23] *Id.* at 60,348 ("The GUARD Model would require manufacturers to pay a GUARD Model rebate payment if the Medicare net price is greater than the GUARD Model applicable international benchmark for a GUARD Model drug. The Medicare net price would be calculated by subtracting manufacturer rebates (obtained from direct and indirect remuneration (DIR)) and discounts (under the Manufacturer Discount Program) from the wholesale acquisition cost (WAC) of the GUARD Model drug. Please see section IV.H. of this proposed rule.").

[24] *See id.* at 60,341, 60,408-411.

[25] 42 U.S.C. § 1315a(b); 90 Fed. Reg. 60,348 ("The GUARD Model rebate payment would be deposited into the Medicare Prescription Drug Account in the Federal Supplementary Medical Insurance Trust Fund.").

C. GUARD Lacks the Requisite "Defined Population" Experiencing "Deficits in Care."

As noted previously, CMS is authorized to test models only where the agency determines that the model addresses a "defined population" for which the agency finds there are "deficits in care leading to poor clinical outcomes or potentially avoidable expenditures."[26] GUARD fails to satisfy this threshold requirement.

CMS purports to address "deficits in care" through GUARD.[27] However, as CMS acknowledges, the GUARD Model "does not directly impact Part D enrollees' out-of-pocket costs for these drugs."[28] Moreover, GUARD does nothing to help patients with the access concerns that actually affect them such as prior authorization requirements and restrictive formulary designs. These real concerns are acutely felt by patients who need ongoing access to 6PC drugs to manage their serious chronic conditions—drugs CMS specifically targets with GUARD.[29] Instead, CMS attempts to identify "deficits in care" to justify GUARD based on beneficiary liability for cost-sharing. Yet, as noted above, high out-of-pocket costs simply are not the case for the vast majority of Medicare beneficiaries.[30] CMS neglects to address how recent reforms, in particular the cap on patients' out-of-pocket drug costs ($2100 for 2026), meaningfully mitigate access concerns related to cost-sharing.[31] Furthermore, more than a quarter of Part D enrollees receive further premium and cost-sharing assistance through the low-income subsidy program, undermining CMS's argument further.[32] Thus, most Medicare beneficiaries do not face cost-sharing burdens that could lead to the "deficits of care" that CMS asserts as the basis for GUARD. Further, CMS concludes that GUARD could potentially have the effect of increasing beneficiary out-of-pocket costs, albeit indirectly through expected changes in manufacturer behavior. The facts on the ground and the agency's own analysis substantially undermine the agency's premise for this model test as a strategy to address deficits in care.

CMS also fails to identify a "defined population."[33] As outlined in the Proposed Rule, GUARD would include beneficiaries who happen to live within randomly selected geographic areas representing 25% of beneficiaries enrolled in a Medicare Part D plan, and who also happen to receive a drug that falls within one of a disparate set of therapeutic categories and meets other specified criteria (e.g., more than $69 million (adjusted annually each performance by the CPI-

[26] *Id.* § 1315a(b)(2)(A).
[27] 90 Fed. Reg. 60,351.
[28] *Id*. at 60,352.
[29] *Medicare Part D's Six Protected Classes Policy: Coverage Policies Create Access Challenges for Patients with Complex Chronic Conditions*, P'SHIP FOR PART D ACCESS (Feb. 2021), https://www.partdpartnership.org/uploads/8/4/2/1/8421729/avalere_report_on_six_protected_classes_--_february_2021.pdf.
[30] *See id.* at 60,351-353.
[31] *See* CTRS. FOR MEDICARE AND MEDICAID SERVS., FINAL CY 2026 PART D REDESIGN PROGRAM INSTRUCTIONS 24 (2026), https://www.cms.gov/files/document/final-cy-2026-part-d-redesign-program-instruction.pdf.
[32] Juliette Cubanski and Anthony Damico, *Key Facts About Medicare Part D Enrollment, Premiums, and Cost Sharing in 2025*, KFF (July 16, 2025), https://www.kff.org/medicare/key-facts-about-medicare-part-d-enrollment-premiums-and-cost-sharing-in-2025/.
[33] *See* 90 Fed. Reg. 60,357.

U) in application-level total gross covered prescription drug spending in the previous year).[34] However, the mere fact that a beneficiary is prescribed and receives a particular drug does not meaningfully identify a "defined population."[35] Under CMS's theory, any randomly sized population of beneficiaries that is prescribed and treated with any randomly selected drug would be a "defined population," rendering the statutory term meaningless.[36]

Further, CMS fails to articulate a reasoned basis for selecting the specific therapeutic classes of drugs that are included as Model drugs. CMS bases its selection of the therapeutic classes of drugs included in GUARD on the misguided notion that the agency's aggregate spending on a set of drugs somehow connects to deficits in care, with no regard to disease incidence, utilization, or actual beneficiary experience with out-of-pocket costs.[37] CMS explains that the agency chose to include USP categories that correspond to the six Medicare Protected Classes of drugs (6PC) in which "all or substantially all" drugs must be covered by Part D plans.[38] And, notwithstanding Congress' clearly articulated priority to protect access to these 6PC drugs, CMS proposes to threaten access and stability to these classes in particular. CMS then notes that "all of the USP selected categories that correspond to [6PC drugs] have 2024 total covered gross drug costs above $1 billion."[39] But it is axiomatic that aggregate spending for these classes of drugs will be substantial given that the drugs in these classes were recognized by Congress as being so crucial for patients to manage their serious chronic conditions that they must be covered by all Part D plans. CMS also proposes to include additional categories of drugs that CMS asserts "correspond to drugs that are used for conditions for which Medicare beneficiaries experience deficits of care and that are within the top spending categories for the Part D Inflation Rebate Program."[40] In identifying these categories, CMS claims (using evidence that largely predates recent Part D reforms that substantially limit out-of-pocket costs) that financially motivated medication non-adherence could "worsen health outcomes."[41] Despite asserted concerns about patients' out-of-pocket costs and access to drugs, CMS nonetheless bases its selection of included therapeutic classes chiefly based on aggregate covered gross drug costs under Part D, with no meaningful correlation to deficits in care and, in fact, a purposeful targeting of drugs for which Congress has afforded more robust protections. This reliance on aggregate spend is, in fact, highly flawed in that it does not translate to beneficiary out-of-pocket costs.

With the agency's principal focus on aggregate drug spending in therapeutic categories, and the proposal to use a rebate strategy that benefits the Medicare trust funds rather than patients, CMS has taken a wholly backwards and impermissible approach to the design of GUARD. That is, instead of addressing a defined population for which there are deficits in care leading to poor

[34] *See id.*
[35] *See id.*
[36] *See id.*
[37] *See id*. at 60,352.
[38] *Id*. at 60,351-352. The 6PC were so identified and codified by Congress to ensure continuous access to life-sustaining medications for patients with high-risk health conditions.
[39] *Id.* at 60,352.
[40] *Id.*
[41] *Id.*

clinical outcomes or potentially avoidable expenditures as required under the statute, CMS has designed GUARD by identifying supposed "potentially avoidable expenditures"[42] without a cogent theory for how those expenditures might result in deficits of care for an ill-defined patient population.[43] Moreover, in the absence of a "defined population" with "deficits in care leading to poor clinical outcomes or potentially avoidable expenditures," GUARD cannot satisfy the statutory requirements for a legitimate model test under section 1115A.[44] Rather, GUARD is an impermissible nationalized drug pricing penalty and government funding mechanism.

D. GUARD Includes No Theory of Quality Preservation or Improvement.

Related to the requirement that a model test address a "defined population" for which there are "deficits in care leading to poor clinical outcomes or potentially avoidable expenditures," section 1115A specifies that "[t]he purpose of [CMMI] is to test innovative payment and service delivery models to reduce program expenditures under the applicable titles while preserving or enhancing the quality of care furnished to individuals under such titles."[45] The statute also specifically requires CMS to assess the "quality of care" provided under a model test to inform the determination of whether the model reduces program expenditures while maintaining or improving the quality of care to Medicare beneficiaries.[46] However, GUARD offers, at most, conjecture as to how reducing (mostly the federal government's) spending for drugs—without altering how care is delivered—could improve or maintain quality. Nor does CMS explain how the agency intends to assess GUARD's effect on quality of care.

CMS offers no colorable theory as to how GUARD will relate to quality of care at all. Rather, CMS offers only a cursory discussion of how the agency might monitor and evaluate whether quality of care improves or is maintained under GUARD before requesting input from the public on "how to structure and monitor quality of care in the GUARD model."[47] Clearly, the capacity of GUARD to preserve or enhance quality of care is dubious given that patients would not receive any direct reduction in their cost-sharing that might plausibly support better medication adherence and improved outcomes. In fact, CMS projects that GUARD might actually have the indirect effect of *increasing* beneficiary cost sharing, making it unlikely that GUARD would be found to meet its obligation to "preserve or enhance" the quality of care for these patients.[48] More broadly, given its harmful effects on the U.S. biotech market and innovation, GUARD would be likely to diminish quality of care by reducing beneficiary access both to existing and

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[42] *Id.* at 60,408.
BIO takes issue as a factual matter with the idea that high drug spend is necessarily an "avoidable expenditure." *Id.* Indeed, the Proposed Rule entirely fails to acknowledge that, in many cases, drug spend is associated with *lower* aggregate expenditures achieved through improved disease management and avoided high-cost interventions including hospitalization.
[43] *Id.* at 60,408.
[44] 42 U.S.C. § 1315a(b)(2)(A).
[45] *Id.* § 1315a(a)(1).
[46] *Id.* § 1315a(b).
[47] 90 Fed. Reg. 60,401.
[48] *Id.* at 60,352.

new therapies, which would make GUARD an impermissible choice for a model test under section 1115A.

Thus, GUARD falls short of the statute's requirement that models must be designed in a way that is expected to preserve or enhance quality of care, subject to assessment as to how the concrete changes being tested will affect the care beneficiaries receive.

E. GUARD's Non-Phased, Mandatory, Effectively Nationwide Approach Exceeds CMS Authority.

As previously noted, CMMI's statute requires the agency to proceed with its model testing in two distinct stages: an initial Phase I test, followed by a Phase II test that is broader in both duration and scope.[49] This phased structure necessarily assumes that the Phase I model test will be meaningfully constrained to ensure an appropriately constructed test that can be evaluated. It also assumes that CMS must complete the initial test before proceeding to Phase II based on the results of the Phase I evaluation.[50] Notably, the statute expressly contemplates that only the Phase II test would operate on a nationwide basis.[51]

In the Proposed Rule, CMS asserts that GUARD will be implemented only in select geographic areas in an attempt to demonstrate that the initiative qualifies as a Phase I model test.[52] But it is doubtful that a mandatory drug-pricing model can, in actuality, be confined to discrete regions. The agency itself anticipates that manufacturers will respond to GUARD by adjusting list prices.[53] Given the nationwide structure of the biotech market, market forces do not support geography- or sector-specific list pricing changes. Rather, any mandatory drug pricing initiative is inherently national in effect. Consequently, even if GUARD's rebate obligations are formally triggered only by utilization of a Model drug by beneficiaries residing in certain locations, GUARD is both designed and expected to influence pricing behavior across the country from the outset. In operation, therefore, even under "Phase I," GUARD functions as de facto Phase II nationwide intervention, impermissibly collapsing the statute's two-phase framework and exceeding the limits Congress placed on CMS's testing authority under section 1115A.

F. GUARD Involves Ultra Vires Use of Waiver Authority.

CMS has no authority to impose new rebates on manufacturers. Recognizing this premise, GUARD purports to obtain this authority by building GUARD on the statutory framework of the Part D inflation rebate. The IRA created a specific, defined inflation rebate regime for Part D under section 1860D-14B of the Social Security Act, a provision limited to recouping price increases above an inflationary benchmark set by Congress. CMS proposes to substantially transform this authority using its waiver authority under section 1115A.

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[49] *See* 42 U.S.C. § 1315a.
[50] *Id.*
[51] *Id.* § 1315a(c).
[52] 90 Fed. Reg. 60,356-57.
[53] *Id.* at 60,353.

However, section 1115A authorizes CMS to waive only such statutory requirements "as may be necessary solely for purposes" of carrying out permissible model tests under this section which, as explained above, GUARD decidedly is not. Section 1115A does not authorize CMS to replace a congressionally chosen substantive parameter with a fundamentally different one, particularly in the absence of an underlying model test.[54]

CMS has proposed waivers that would go far beyond "waiving" statutory requirements, and instead simply convert the statute into a completely different one. Specifically, in the Proposed Rule, CMS does not relax or suspend a statutory requirement, but rather creates an entirely new rebate out of whole cloth. CMS then layers this new rebate on top of the rebate—based on U.S. inflation—chosen by Congress. In sum, not only has CMS not really waived the underlying inflation rebate requirements, which still apply, the agency has added a wholly new rebate based on an international reference price construct totally unrelated to U.S. inflation, thereby transforming the nature of the rebate statute.

The repurposing of an entire statutory program in this manner is not a permissible waiver and represents an ultra vires assertion of authority beyond what is granted in section 1115A. The Supreme Court has rejected the notion that agency waiver authority is limitless, denouncing the use of waiver authority to "create[] a novel and fundamentally different" program from the underlying statute.[55] The agency's action is particularly troubling here given that the international reference pricing metric CMS now proposes to "test" is one that was specifically considered and soundly rejected by Congress just over three years ago.[56]

G. GUARD's Scope Impermissibly Extends Beyond Statutory Limitations to Specific Federal Programs.

CMS's authority under Section 1115A is confined to testing payment and service delivery models within Medicare, Medicaid, and CHIP.[57] CMS nevertheless expects that the imposition of this mandatory Model will induce manufacturers to modify their prices across the board.[58] These anticipated pricing responses are, by design, not limited to the specified federal programs, or even federal programs more generally, but instead reach into commercial and other non-covered markets within and outside of the U.S. CMS has no authority to unilaterally control drug pricing in commercial and non-covered markets. [59] Yet that is precisely what GUARD would do.

Under comparable circumstances, the D.C. Circuit struck down a CMS rule that relied on a Medicare-specific authority but had an intended effect that extended well beyond the scope of

[54]*See* 42 U.S.C. § 1315a.
[55]*Biden v. Nebraska*, 143 S. Ct. 2355 (2023).
[56]*See e.g.,* Christen Linke Young et al., *International Reference Pricing for Prescription Drugs*, BROOKINGS (July 9, 2025), https://www.brookings.edu/articles/international-reference-pricing-for-prescription-drugs/.
[57]42 U.S.C. § 1315a.
[58] *See* 90 Fed. Reg. 60,353, 60,411.
[59]*See generally* 42 U.S.C. §1315a.

the program.[60] At issue in that case was a rule requiring drug manufacturers to disclose a drug's wholesale acquisition cost in television advertisements. While CMS claimed the regulation was intended to benefit Medicare patients, the court found that HHS "acted unreasonably in construing its regulatory authority to include the imposition of a sweeping disclosure requirement that is largely untethered to the actual administration of the Medicare or Medicaid programs."[61] Likewise here, by designing a mandatory intervention whose foreseeable effects extend well beyond specified statutory limitations to specified programs—in this case Medicare, Medicaid, and CHIP—CMS exceeds the statutory boundaries established by Congress.

H. GUARD Purports to Unilaterally Make Policy Decisions Reserved for Congress Under the Major Questions Doctrine.

The Supreme Court has made clear that courts "presume that Congress intends to make major policy decisions itself, not leave those decisions to agencies," and that an agency asserting such power must identify "clear congressional authorization."[62] In fact, the Court affirmed this principle just days ago, reminding that in several cases involving "major questions," the Court has reasoned that "both separation of powers principles and a practical understanding of legislative intent" suggest that Congress does not delegate "highly consequential power" through ambiguous language.[63] While Congress has delegated authority to CMS to test payment and service delivery models, there is no evidence, let alone the requisite clear signal, that Congress contemplated the use of this authority to issue mandatory models that have the effect of unilaterally setting drug prices for patients throughout the U.S.—a question of major economic significance.[64]

In fact, Congress has legislated directly and extensively over many decades in the biopharmaceutical field.[65] Extensive Congressional action in this area illustrates a basic characteristic of constitutional structure: when Congress chooses to regulate through legislation, it also intends to constrain the discretion of the executive branch. Importantly, a common thread that runs through the decades of Congressional action in the biopharmaceutical field is exclusive reliance on information and market dynamics within the

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[60] *Merck & Co., Inc. v. U.S. Dept. of Health and Human Services*, 962 F.3d 531, 533 (D.C. Cir. 2020).
[61] *Id.*
[62] *West Virginia v. EPA*, 597 U.S. ___, slip op. at 19 (2022).
[63] *Learning Resources, Inc., et al. v. Trump*, et al., No. 24–1287, slip op, S. Ct. (Feb. 20, 2026).
[64] There is likewise no clear signal that Congress contemplated use of this authority to make participation in a test of a payment or delivery model *mandatory*. The mere authority to develop and conduct a test, which Section 1115A provides, does not either logically or by necessity encompass the power to compel participation. CMS's own expectations of GUARD impact leave no doubt that the models have vast economic and political significance. The power to mandate participation in such a costly and disruptive endeavor would need to be clearly communicated by Congress, not assumed by CMS. Section 1115A, which is silent on the issue, simply does not do that.
[65] *See*, *e.g.*, Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (establishing Medicare Part D); Patient Protection and Affordable Care Act, Pub. L. No. 111-148, 124 Stat. 119 (2010) (reforming Medicare Part D and the Medicaid Drug Rebate Program and establishing a pathway for biosimilars, and other measures); 21st Century Cures Act, Pub. L. No. 114-255, 130 Stat. 1033 (2016) (making reforms to FDA approval processes); Bipartisan Budget Act of 2018, Pub. L. No. 115-123, 132 Stat. 64 (making further reforms to coverage and manufacturer discounts in Part D).

U.S. GUARD, however, casts these considerations aside, including the protection of patent rights that are central to U.S. biotech investment and innovation. Instead, GUARD imposes mandatory rebates on virtually all single-source drugs in the identified categories from the moment they enter the market using a foreign pricing construct that Congress has previously considered and roundly rejected.[66]

Through GUARD, CMS substitutes its own policy preferences for Congress's long-standing, calibrated statutory choices made through decades of drug pricing laws, as well as through the CMMI statute. In doing so, CMS vastly expands the scope of government price constraints without the clear statement of authority that would be necessary to displace Congressional intent to reserve to itself the authority to regulate in the area of drug pricing.

GUARD also runs contrary to certain critical patient protections established by Congress for purposes of Medicare Part D. To protect patient access to critical therapies, Congress codified the 6PC of drugs that Part D plans must cover—antidepressants, antipsychotics, anticonvulsants, immunosuppressants for treatment of transplant rejection, antiretrovirals, and antineoplastics.[67] Congress protected the 6PC to ensure beneficiaries with the complex, chronic, or life-threatening conditions treated by drugs in these classes have uninterrupted access to necessary medications, preventing high-risk therapeutic interruptions—implicitly recognizing the critical nature of these medications for patients. GUARD would subject all qualifying drugs in the 6PC to international benchmarks and rebates without any clear Congressional authorization and, in doing so, could undermine Congressional intent to preserve patient access to these statutorily mandated drug categories while discouraging innovation in the very therapeutic areas where Congress expressly endeavored to protect access.

It would be one thing for GUARD to overwrite these carefully constructed policies if Congress had expressly authorized CMMI to establish broad drug policy. But it did not. Instead, Congress granted CMS a circumscribed authority to test *payment and service delivery models*. Setting aside the fact that GUARD is neither a test nor a payment and service delivery model under section 1115A, as described above, nothing in section 1115A supplies the clear statement required for CMS to unilaterally reshape national drug pricing policy and influence international drug pricing policy as contemplated in GUARD.[68] CMS's own expectations of GUARD impact leave no doubt that the models have vast economic and political significance. The power to mandate participation in such a costly and disruptive endeavor would need to be clearly communicated by Congress, not assumed by CMS. And it is doubtful Congress intended CMS to use the cabined authority under section 1115A to disrupt the balances carefully struck by Congress through years of federal regulation of drugs and biologics by adopting policies wholly antithetical to the existing statutory drug approval and pricing apparatus.

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[66] *See e.g.,* Christen Linke Young et al., *International Reference Pricing for Prescription Drugs*, BROOKINGS (July 9, 2025), https://www.brookings.edu/articles/international-reference-pricing-for-prescription-drugs/.

[67] 42 U.S.C. § 1395w-104(b)(3)(G)(iv).

[68] *See* 42 U.S.C. § 1315a.

III. GUARD Violates Federal Appropriations Laws.

GUARD violates not just CMS's own statutory authority, but foundational constitutional and statutory restrictions that protect Congress's exclusive power of the purse. GUARD would compel manufacturers to make new payments to the Medicare Supplementary Medical Insurance (SMI) Trust Fund—without any statute that authorizes those collections—thereby unlawfully supplementing federal funds in a manner CMS has no power to waive.[69]

Federal fiscal law generally bars the augmentation of appropriations: agencies may not increase the funds available to them by collecting money from outside sources unless Congress clearly authorizes it.[70] That principle flows from Article I, Section 9 of the Constitution, which provides that "[n]o Money shall be drawn from the Treasury, but in Consequence of Appropriations made by Law."[71] And it has been codified in several fiscal statutes—including the Miscellaneous Receipts Act, which requires officials who receive money "for the Government" to deposit it into the general fund of the Treasury (absent a specific statutory direction to the contrary),[72] and the Anti-Deficiency Act, which bars obligating funds in advance of or in excess of appropriations.[73] Here, GUARD impermissibly directs new incremental rebate payments into the SMI Trust Fund rather than the Treasury's general fund, effectively boosting the Trust Fund's available resources without congressional authorization—an end-run around Congress's power of the purse.[74]

Nothing CMS cites supplies that missing authority. Section 1115A allows CMS to test models and to waive limited Social Security Act provisions as necessary for testing; it does not confer revenue-raising power or authorize CMS to disregard appropriations statutes.[75] And CMS cannot bootstrap this result from the inflation rebate provisions it purports to "waive"—which authorize only a specific, inflation-based rebate formula, not the MFN-style payments CMS seeks to impose.[76]

IV. GUARD Raises Significant Constitutional Issues.

A. GUARD Raises Serious Questions Under the Presentment Clause, the Separation of Powers, and Non-Delegation Doctrine.

Through GUARD, CMS asserts unilateral power to establish mandatory nationwide drug pricing without any meaningful limiting principle supplied by Congress. That is an unconstitutional interpretation of section 1115A.

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[69] *See* 90 Fed. Reg. 60,340.
[70] *See*, *e.g.*, *Applicability of the Miscellaneous Receipts Act to an Arbitral Award of Legal Costs*, 42 Op. O.L.C. 30 (Mar. 6, 2018).
[71] U.S. CONST. art. I, § 9, cl. 7.
[72] 31 U.S.C. § 3302(b).
[73] 31 U.S.C. §§ 1341–42.
[74] *See Scheduled Airlines Traffic Offices v. Dept. of Defense*, 87 F.3d 1356, 1362 (D.C. Cir. 1996).
[75] *See* 42 U.S.C. § 1315a.
[76] *See* 42 U.S.C. § 1395w-3a(i); 42 C.F.R. § 427.10.

Section 1115A authorizes CMS to engage in bounded experimentation in the context of payment and service delivery for specified purposes; it does not furnish standards for the broad regulation by CMS of drug prices in the U.S..[77] As the Supreme Court has explained, "Congress must 'lay down by legislative act an intelligible principle to which the person or body authorized to [act] is directed to conform.'"[78] Here, Congress has established limiting principles within section 1115A. Yet, as described in Section I of this letter, with GUARD, CMS interprets the statute to completely ignore those limiting principles, and in doing so identifies no "intelligible principle" governing its actions.

Further, if section 1115A could be given the interpretation CMS asserts in the GUARD Proposed Rule, Congress would have impermissibly delegated essential legislative functions rooted in Article I, Section I of the U.S. Constitution to allow the agency unfettered authority, without further legislative consideration, to rewrite the Medicare statute as it wishes including the mandatory imposition of a nationwide drug-pricing policy of broad scope and duration. Read this way, Section 1115A would transfer core legislative authority to the executive branch, exceeding the Constitutional limits on delegation.

That interpretation likewise would permit CMS to unilaterally rewrite congressional enactments in violation of the Presentment Clause of Article I, which sets forth a mandatory procedure—passage by both congressional chambers and presentment to the President—for the enactment of any law.[79] As the Supreme Court has recognized, the Presentment Clause forbids "unilateral [Executive] action that either repeals or amends parts of duly enacted statutes."[80] Yet under CMS's view, its statutory testing and waiver authority provides free license to amend statutory rebate provisions—"rejecting the policy judgment made by Congress and relying on [CMS's] own policy judgment."[81] Just like the Line Item Veto Act struck down in *Clinton v. City of New York*, section 1115A cannot permissibly be read to authorize such statutory rewrites.

B. GUARD Violates Due Process.

The Due Process Clause of the Fifth Amendment of the U.S. Constitution forbids the government from depriving persons of property without due process of law.[82] GUARD would violate procedural due process protections afforded under the Constitution, under the guise of a section 1115A model test, in several ways.

GUARD imposes mandatory, economically coercive pricing constraints for broadly construed international analog drugs using international reference price benchmarks. CMS would unilaterally establish the international analog drugs and pricing benchmarks with no meaningful opportunity for review or reconsideration of either.

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[77] *See* 42 U.S.C. § 1315a.
[78] *Gundy v. United States*, 588 U.S. 128, 135 (2019).
[79] U.S. Const. art. I, § 7, cl. 2.
[80] *Clinton v. City of New York*, 524 U.S. 417, 438 (1998).
[81] *Id.* at 444.
[82] U.S. CONST. amend. V.

As described in more detail below, the "Method I" or "default international" benchmark would be ostensibly based on CMS's scan of an unspecified panoply of sources of international reference pricing data.[83] CMS would use data from one or more sources, undisclosed to the manufacturer, and collected before the launch of GUARD—in some cases even before issuance of the Proposed Rule. This arbitrary and undisclosed "black box" calculation would be unreviewable and remain in place throughout the duration of GUARD. CMS also provides an alternative "Method II" or "updated international" benchmark calculation that would be based on international reference pricing and sales data submitted to CMS by the manufacturer.[84] Similarly, there is no opportunity for review or reconsideration of CMS's determinations on this calculation.[85] Moreover, as explained below, Method II represents a false choice, and most manufacturers would be forced to accept the CMS determination under Method I without recourse. The use of an international reference price benchmark in the collection of rebates under GUARD that is unilaterally established by CMS without notice or opportunity for review deprives manufacturers of property rights in their products in violation of the procedural due process protections afforded to manufacturers under the Constitution.

Based on the unreviewable international benchmark price calculation, unilaterally established by CMS, GUARD further imposes a system of rebates that manufacturers would be required to pay to CMS reflecting the difference between the U.S. and benchmark price. CMS would calculate these rebates, notify manufacturers of the amounts due and conduct a quarterly reconciliation process. While there are some nominal procedural protections within this rebate calculation and reconciliation process, given the dearth of information available to the manufacturer to evaluate CMS rebate calculations, these protections are wholly insufficient. In testing other CMMI models, CMS ordinarily invokes the extensive procedural review and reconsideration regulations the agency has issued for that purpose.[86] These regulations offer robust procedures for the exchange of information between CMS and model participants, and a meaningful process for review and reconsideration. In GUARD, CMS casts aside the ordinary protections afforded to CMMI model participants in favor of procedures that parallel the IRA's Part D inflation rebate program. In doing so, CMS deprives manufacturers that are mandatory participants in GUARD of usual procedural protections and leaves them with no meaningful procedural protections, thereby depriving them of protected property interests in their patented products and the expected returns on those products without a Constitutionally sufficient process.

C. GUARD Represents an Unconstitutional Taking.

The Takings Clause of the U.S. Constitution prohibits the government from appropriating private property for public use without just compensation.[87] This protection extends beyond real property to intangible property rights, including patents, which the Supreme Court has

[83] *See* 90 Fed. Reg. 60,359-360.
[84] *See id*.
[85] *See id.* at 60,341, 60,348.
[86] 42 C.F.R. § 512.190.
[87] U.S. CONST. amend. V.

repeatedly recognized as a constitutionally protected property interest.[88] Accordingly, government action that destroys or appropriates this right, such as by compelling access or dictating price, implicates the Takings Clause.[89]

By conditioning practical participation in the federal Medicare program on acceptance of government-imposed prices well below U.S. market levels, effectuated through a rebate scheme, GUARD compels manufacturers to supply patented drugs on nonconsensual terms, in some cases immediately upon launch. Further, GUARD effectuates these prices through the collection of rebates from manufacturers that are deposited into the Medicare Trust Funds. GUARD thus effects a forced transfer of protected property interests for public benefit without compensation.

Even when the court finds that a physical taking has not occurred—meaning that the government has not physically appropriated or occupied specific property—courts have recognized regulatory takings when "regulation goes too far."[90] Specifically, takings liability may attach when regulation in questions substantially interferes with "reasonable investment backed expectations."[91]

D. The Foreign Commerce Clause Gives Congress Alone the Power to Regulate Commerce with Foreign Nations.

Article I, Section 8, Clause 3 of the U.S. Constitution vests in Congress, not the executive, the power to regulate commerce with foreign nations.[92] While Congress can choose to delegate aspects of this power to the Executive Branch, there has been no such delegation to CMS through Section 1115A or otherwise. The Administration has repeatedly stated that its drug-pricing initiatives are intended not only to lower prices domestically but also to exert upward pressure on prices abroad.[93] By setting Medicare payment levels based on prices established by foreign governments and foreign-domiciled companies, with no required nexus to the U.S., GUARD is structured and intended to directly influence manufacturers' global pricing strategies. Specifically, price increases for the Model drug in reference countries would operate to increase

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[88]*See Horne v. Dept. of Agric.*, 576 U.S. 350, 359-360 (2015) (citing *James* v. *Campbell*, 104 U. S. 356, 358 (1882)) ("[A patent] confers upon the patentee an exclusive property in the patented invention which cannot be appropriated or used by the government itself, without just compensation, any more than it can appropriate or use without compensation land which has been patented to a private purchaser.").

[89]*See id.*

[90]*See Penn Central Transportation Co. v. New York City*, 438 U.S. 104, 124 (1978)*; see also id. Pennsylvania Coal Co. v. Mahon*, 260 U. S. 393, 260 U. S. 415 (1922). (stating that when "regulation goes too far, it will be recognized as a taking.").

[91]*See id; see also Kaiser Aetna v. United States*, 444 U.S. 164 (1979), *Pruneyard Shopping Ctr. v. Robins*, 447 U.S. 74 (1980).

[92]U.S. CONST. art. I, § 8, cl. 3.

[93]*Fact Sheet: President Donald J. Trump Launches TrumpRx.gov to Bring Lower Drug Prices to American Patients,* THE WHITE HOUSE (Feb. 5, 2026), https://www.whitehouse.gov/fact-sheets/2026/02/fact-sheet-president-donald-j-trump-launches-trumprx-gov-to-bring-lower-drug-prices-to-american-patients/. ("President Trump is delivering on promises to ensure American patients no longer pay high prices to subsidize low prices in the rest of the world, something the political establishment did not believe was possible.").

the manufacturer's Method II benchmark price and thereby reduce a manufacturer's GUARD rebate liability. Thus, as structured by CMS, GUARD would operate as an instrument of foreign economic regulation in violation of the foreign commerce clause. GUARD could also reach further into foreign commerce by influencing manufacturer negotiations with foreign nations and impacting manufacturer decisions about whether to enter or remain in foreign markets. Therefore, as envisioned by CMS, GUARD would represent an agency instrument of foreign economic regulation that is not authorized by Congress, beyond the scope of CMS authority to test models under section 1115A, and in violation of the foreign commerce clause.

E. GUARD Conflicts with the Scheme of Patent Laws Established Under the Patent Clause.

The Patent Clause of the U.S. Constitution, along with the intellectual property regimes created by Congress, create an intentional scheme to reward U.S. innovation by granting manufacturers a time-limited right to earn returns at a price the market will pay for their patent-protected products. [94] By imposing administratively established, below-market benchmark prices on patented products before patent expiration or, in some cases, the end of FDA-granted exclusivities, GUARD is at direct odds with this Constitutional scheme. Courts have recognized that price-control regimes targeting patented goods may conflict with the scheme of patent laws, suggesting that such controls can be at odds with the structure and objectives of federal patent policy.[95]

V. Many Elements of GUARD Run Afoul of Other Statutory Requirements, Including the Administrative Procedure Act.

A. CMS Lacks Authority to Impose the Proposed Civil Monetary Penalties.

CMS proposes to impose civil monetary penalties under section 1860D-14B(e) of the Act by "rely[ing] on" section 1128A of the Act if a manufacturer fails to comply with the GUARD Model requirements.[96] However, administrative agencies do not have independent authority to impose civil penalties; such authority can only be granted by Congress.[97] There is no hint of authority for CMS to invoke civil monetary penalties in the context of any model, much less a mandatory one, within the statutory scheme of section 1115A. Moreover, CMS cannot compel compliance with model tests under section 1115A through the background authority under section 1128A of the Act to impose penalties for knowingly false claims and delegated to the Department of Health & Human Services Office of the Inspector General rather than CMS.[98] In the absence of any authorization from Congress, CMS's authority to waive statutory requirements solely for

[94] U.S. CONST. art. I, § 8, cl. 8. *See*, *e.g.*, U.S. Code, Title 35.
[95] *See*, *e.g.*, *Biotechnology Industry Organization v. District of Columbia*, 496 F.3d 1362 (Fed. Cir. 2007) (affirming injunction of D.C. drug price-control statute as preempted by federal patent law).
[96] 90 Fed. Reg. 60,400.
[97] *See*, *e.g.*, *Atlas Roofing Co. v. OSHRC*, 430 U.S. 442 (1977); *Helvering v. Mitchell*, 303 U.S. 391 (1938); *Lloyd Sabaudo S.A. v. Elting*, 287 U.S. 329 (1932).
[98] *See*, *e.g.*, Grants, Contracts, and Other Agreements: Fraud and Abuse; Information Blocking; Office of Inspector General's Civil Money Penalty Rules, 88 Fed. Reg. 42,820, 42,821 (Jul. 3, 2023).

purposes of model tests under section 1115A does not allow CMS to reach outside the scope of a model test to invoke punitive authorities granted by Congress against mandatory model participants that fail to follow model test requirements.

Moreover, the GUARD rebates operate as unauthorized sanctions rather than a permissible waiver under section 1115A solely for purposes of a Phase I model test. The APA draws a clear line: an agency may not impose a "sanction"—a term that encompasses penalties and fines—unless Congress has delegated jurisdiction and authorized the sanction by law. The APA provides that "[a] sanction may not be imposed . . . except within jurisdiction delegated to the agency and as authorized by law."[99] With GUARD, CMS would compel manufacturers to make mandatory payments untethered to any statutory rebate obligation and enforce them through an inapplicable civil penalty scheme. Section 1115A contains no clear statement authorizing CMS to levy penalties of this kind through a "model," and the GUARD rebate mechanism therefore falls outside CMS's lawful authority.

B. The Proposed Pricing Policies in GUARD are Arbitrary and Capricious, Particularly Given CMS's Failure to Consider Key Issues.

Under the Administrative Procedure Act (APA), an agency must "articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made."[100] Any failure to do so is arbitrary and capricious, and the agency action must be set aside.[101] GUARD rests on a host of haphazard and unexplained policy choices that—if finalized as proposed—would be arbitrary and capricious in violation of the APA.[102] Further, as discussed below, given the lack of detail and enormous number of open questions CMS offers in proposing GUARD, CMS fails to provide adequate notice to the extent that the agency cannot possibly fill in the blanks and answer questions in a way that could be anticipated by the public.

As outlined in the Proposed Rule, GUARD would rely on foreign drug pricing to establish mandatory rebates under Medicare. As a threshold matter, imposing the use of international reference pricing for this purpose, outlined in the Proposed Rule, is likely to produce arbitrary results, as such data are generally opaque, highly variable, and often protected by complex confidentiality regimes. These features further undermine that CMS is conducting a legitimate "test" of some identified hypotheses, as Section 1115A requires.

In one particularly egregious example of CMS's neglect to consider the intrinsic market realities underpinning GUARD, CMS does not acknowledge or consider the prevalence of parallel trade in either of the proposed benchmark "alternatives." Parallel trade—lawful in the European Union (EU) countries which are heavily represented in the reference countries CMS proposes, is a phenomenon whereby a patented product is diverted from the original distribution chain to another one, often through a transfer from the supply chain in one EU member state to an

[99] 5 U.S.C. § 558(b).
[100] *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (quotation omitted).
[101] 5 U.S.C. § 706.
[102] *Id.*

entirely different member state where the product then competes with the original distribution chain through a parallel distributor.[103] This practice occurs due to a confluence of factors that create incentives for alternative distributors and contribute to vast price differentials across markets, varying price control policies and market demands, combined with the low cost and regulatory ease of moving products across EU member state borders.[104] Widespread parallel trade may result in downward pressure on reference country prices and is largely outside the control of the manufacturer. Failure to consider parallel trade practices and their influence on reference country prices, as well as the lack of any control manufacturers can exercise over these practices and the resulting downward price pressures that may impact pricing data pulled by CMS, shows a marked failure by CMS to offer a rational connection between highly relevant facts and the choices CMS proposes for GUARD; and thus, is arbitrary and capricious.

More specifically, the methodologies CMS outlines in the Proposed Rule for identification of international analog drugs and establishing benchmark price are deeply flawed and fail to consider key issues.

CMS proposes to identify international analog drugs by reference to active ingredient, route of administration, dosage form, and strength. CMS fails to explain why these drug attributes are probative of "sameness" in drugs in the U.S. and the ex-U.S. Beyond this, even if two drugs were not aligned across these stated characteristics, CMS proposes to conduct further review to determine whether any differences are "insignificant." In this manner, CMS has proposed a limitless universe of international drugs that could be analogs, offering no principled constraints on the agency's ability to compare two entirely different drugs and assess financial penalties in the U.S. based on a completely different drug. This approach is impermissibly arbitrary and capricious agency conduct. While it is unclear whether this is CMS's intent, this approach would be particularly arbitrary were CMS to identify an analog for a U.S. drug that is not sold overseas at all, as there can be no international analog for a drug marketed and sold in the U.S. if the owner of the U.S. drug neither sells its drug outside the U.S. or licenses it for sale outside the U.S.

CMS further proposes inconsistent rationales for excluding particular ex-U.S. drugs, noting that it would exclude as comparators ex-U.S. drugs that are regarded as generics under their relevant regulatory authorities. CMS fails to recognize that the agency would need to *also* exclude the brand drug that serves as a reference for those generic drugs, if this could even be a workable approach. CMS states, "[b]y excluding international generics and international biosimilar biological products among international products, CMS aims to keep the differences between the GUARD Model drugs—which do not include any generics or biosimilar biological products—and their set of international analogs as limited as possible to just the country of sale and price. CMS believes that this is reasonable because it means there are no generics or biosimilar biological products among either the GUARD Model drugs or the corresponding set of

[103]Joan Costa-Font, *Is Medicines Parallel Trade 'Regulatory Arbitrage'?*, 16(4) INT. J. HEALTH ECON. MANAG., 321-36 (2016), https://pmc.ncbi.nlm.nih.gov/articles/PMC6116900/.
[104]Jacob Arfwedson, *Parallel Trade in Pharmaceuticals*, INST. FOR POLICY INNOVATION (July 15, 2004), https://www.ipi.org/ipi_issues/detail/parallel-trade-in-pharmaceuticals.

international analogs."[105] However, this approach would not ensure no generics or biosimilar drug products are included in GUARD because it neglects to exclude the brand drug for which there are foreign generics—as a brand drug with generic competition would be excluded from GUARD in the U.S.

Further, CMS identifies two alternative international reference price benchmarks for use in GUARD, both of which are technically problematic and impermissibly arbitrary and capricious. In fact, CMS concedes that both of its proposed methods would involve substantial uncertainty.[106]

First, for "Method I," CMS would establish a one-time default benchmark international reference price at the outset using data that may predate initiation of GUARD.[107] CMS neglects to recognize, including in its impact analysis, that many of these sources are proprietary and would be costly for manufacturers to access. CMS does not describe a robust data validation procedure or meaningfully limit the data to drugs with the same formulation, indications, dosage and presentation. In fact, in certain cases where an exact strength match is not available, CMS would identify an international "analog" to a U.S. product that has markedly different characteristics in terms of dosage strength, labeling requirements, and patient populations.[108] And, in some cases, the data sources CMS has proposed to rely on no longer exist.[109]

Nor does CMS provide any review, reconsideration, or appeal process if manufacturers find that third-party pricing data are inaccurate or not comparable in terms of reference product (e.g., where the international analog does not share the same formulation, indication(s), dosage, and/or presentation).[110]

Despite acknowledging potential gaps and inconsistencies in available data, CMS asserts that existing sources are "adequate" to establish country-level averages.[111] Alarmingly, at least one of the sources CMS identifies has previously notified CMS that its international drug pricing data are "not suitable for calculation of actual adjustments in pricing or reimbursement."[112] This point is concretely illustrated by reports from several BIO member companies that some of the databases CMS references for GUARD include prices for drugs in countries where those drugs have not been approved for reimbursement and, in some cases, have never been sold. Additionally, in reviewing some of the databases referenced in GUARD, we found that even within a single database, the methodology used to determine the price of a single drug varies

[105] 90 Fed. Reg. 60,380.
[106] *Id.* at 60,353, 60,411.
[107] *Id.* at 60,378.
[108] *Id.* at 60,379.
[109] The CIA World Factbook, cited as the proposed source for country GDP data, will no longer be published as of February 4, 2026. *Spotlighting The World Factbook as We Bid a Fond Farewell*, CENT. INTEL. AGENCY (Feb. 4, 2026), https://www.cia.gov/stories/story/spotlighting-the-world-factbook-as-we-bid-a-fond-farewell/.
[110] *See* 90 Fed. Reg. 60,406.
[111] *Id.* at 60,360. ("CMS believes the existing data sources are adequate for purposes of identifying country-level average prices.").
[112] IQVIA, CMS Most Favored Nation (MFN) Model (CMS-5528-IFC), Docket No. CMS–2018–0132-2750 (Jan. 26, 2021), https://www.regulations.gov/comment/CMS-2018-0132-3860.

significantly from country to country. Use of these databases would be an inconsistent approach that would produce inconsistent results between and among manufacturers and Model drugs. Still, CMS describes how it intends to cobble together international reference prices from an unspecified array of sources—providing only potential examples and no authoritative list nor any definitive ranking of sources. [113] There is no way for a manufacturer to know which source or combination of sources would be used, or to dispute the agency's final, one-time determination of this benchmark price. Moreover, default benchmarks can be set using data from as early as January 1, 2024—well before manufacturers were made aware of the Proposed Rule and without any opportunity for manufacturers to contest those data.

A framework that turns on pricing inputs the agency admits may be inaccurate renders the resulting payment levels so indeterminate and unpredictable as to be arbitrary and capricious.

Perhaps recognizing the glaring flaws in the Method I approach, or perhaps intentionally leveraging the flawed Method I approach to coerce manufacturers to submit their own proprietary pricing information, CMS then offers to calculate an alternative benchmark price under "Method II." However, this "alternative" approach is equally flawed and does not represent any real alternative.

As a preliminary matter, CMS fails to provide any assurances to manufacturers that their net pricing information—which necessarily includes confidential, proprietary trade secrets—will not be used for other purposes, disclosed to other government entities, or otherwise made vulnerable to public disclosure. As CMS is well aware, release of such information would cause manufacturers serious, irreparable harm to protected privacy and business interests.

A closer look at the CMS Method II approach also reveals fundamental and incurable flaws. Manufacturers' disclosure to CMS of proprietary ex-U.S. pricing and sales information is not only unreasonable, it is in many instances unlawful, or infeasible due to contractual confidentiality limitations. Importantly, many manufacturers, especially small and mid-sized manufacturers, do not control or have access to international pricing or sales information because analog products are out-licensed, co-commercialized, or sold through affiliates or third-party partners outside the U.S.

As just one example, a BIO member that is now a midsized biotech based in Wilmington, Delaware, is in this very situation. In 2009, the company was developing a therapy to treat patients with a rare blood cancer. As a then small biotechnology company with operations and workforce based entirely in the U.S., and without the scale to commercialize their drug globally, the company licensed its ex-U.S. rights to a large multinational manufacturer in 2009, two years before FDA would grant first approval of their drug and 17 years before GUARD would be proposed. Rather than enabling the company to avoid what were at the time unforeseeable future price comparisons across nations, this licensing supported the company's continued development and U.S. commercialization of their drug, as well as reinvestment of resulting revenues into domestic research and development. However, as part of that agreement, the

[113] 90 Fed. Reg. 60,353, 60,411.

company ceded authority over ex-U.S. pricing decisions; and the company has never set or controlled prices for their drug outside the U.S. throughout the duration of the agreement. The licensing agreement signed nearly 20 years before CMS proposed GUARD could not have contemplated the need for the company to have data rights sufficient to calculate a price under Method II.

It is highly doubtful that manufacturers have the discretion or capability to gather the requisite information envisioned for Method II across the spectrum of global reference countries. Moreover, it would be patently unfair, arbitrary, and capricious to penalize manufacturers based on ex-U.S. pricing decisions over which they have no control and using data into which they have no visibility. Given the insurmountable barriers involved in submitting ex-U.S. information to CMS, Method II presents a false choice that would force manufacturers to live with whatever reference values CMS might produce under its deeply flawed, arbitrary and capricious, Method I approach.

C. CMS Provides Insufficient Notice Regarding Multiple Aspects of GUARD, Depriving the Public of Meaningful Opportunity to Comment

CMS abjectly fails to meet requirements for notice-and-comment rulemaking under the APA[114] and section 1871 of the Social Security Act in proposing GUARD.[115] In particular, CMS is strictly obligated under section 1871 of the Act to engage in notice-and-comment rulemaking to establish Medicare payment policies.[116] Adequate notice to the public of proposed policies is foundational to notice-and-comment rulemaking because, without it, the public has no meaningful opportunity to comment on the proposal.[117] Specifically, agencies must provide enough detail in the notice of proposed rulemaking to allow the public to appreciate and assess the proposal, and meaningfully comment on it.[118] Further, in the absence of adequate public notice, CMS is precluded from finalizing policies in a final rule.[119]

CMS fails to provide sufficient information in the Proposed Rule to afford the public, including BIO and its members, a meaningful opportunity to comment on key aspects of GUARD. In two poignant examples, CMS omits specifics about how the agency intends to address overlaps between GUARD and other Trump Administration initiatives including through CMS and CMMI, and, as discussed above, whether or how CMS intends to use various information sources to identify ex-U.S. "analogs" and establish a Method I international benchmark reference price for Model drugs.

Specifically regarding overlaps, CMS "welcome[d] comments on the potential ways the proposed GUARD Model may impact CMS programs and initiatives and the potential need for

[114] 5 U.S.C. § 553 (2024).
[115] 42 U.S.C. § 1395hh.
[116] *See Azar v. Allina Health Services*, 139 S. Ct. 1804 (2019).
[117] *See*, *e.g.*, *WJG Tel Co., Inc. v. FCC*, 675 F.2d 386, 389 (D.C. Cir. 1982); *see Fla. Power & Light Co. v. Nuclear Regulatory Comm'n*, 846 F.2d 765, 771 (D.C. Cir. 1988).
[118] *See*, *e.g.*, *National Lifeline Ass'n v. FCC*, 921 F.3d 1102, 1116 (D.C. Cir. 2019).
[119] *Id.*

modifications or adjustments to the proposed GUARD Model that may be necessary to minimize model overlap impacts."[120] The public should not be left to guess about what CMS could potentially envision or prioritize with respect to overlaps with GUARD. It is simply not possible to comment on this topic given that CMS has not provided a specific overlaps policy to which the public could react. The only inkling CMS provides of a potential overlaps policy is the following text, buried in the regulatory impact analysis: "If certain manufacturers were excluded due to interactions with other CMS Innovation Center models or for any other reason, the impacts from this proposed demonstration could be significantly less than described in this analysis."[121] This is hardly enough detail to inform meaningful comment.

As discussed above, to establish the single Method I benchmark price for a GUARD Model drug, CMS would refer to an unspecified, undefined, and unbounded set of potential sources for reference pricing information in reference countries.[122] CMS would then choose data from among one or more of these sources, which might or might not include pricing information from all reference countries, and might or might not use a consistent approach to reporting within or among sources, and plug it into the agency's black box calculator to produce a single benchmark value.[123] In short, the public remains in the dark as to the agency's plans and vulnerable to the agency's post hoc choices.[124]

Given the absence of key details provided in proposing GUARD, it will not be possible for CMS to address these and other missing pieces in a way that could be anticipated by the public. Further, in the absence of specific proposals from CMS, the agency does not, because it cannot, provide a sufficient impact analysis.[125] As such, CMS has provided the public insufficient information on the proposal and its expected impacts to allow a meaningful opportunity to comment on GUARD.

D. Transformational Industry-Wide Impacts Violate the Affordable Care Act's "Access to Therapies" Mandate.

In the Affordable Care Act, the very law that enacted section 1115A, Congress included a directive that, notwithstanding any other provision of the Act, CMS is prohibited from issuing any regulation that *inter alia* creates any unreasonable barriers to the ability of individuals to obtain appropriate medical care, impedes timely access to health care services, or limits the availability of health care treatment for the full duration of a patient's medical needs.[126] By upending Congressional intent and disrupting settled expectations regarding U.S. drug pricing policy, GUARD would violate this directive. The impact of importing international reference

[120] 90 Fed. Reg. 60,405.
[121] *Id.* at 60,409.
[122] *Id.* at 60,359-361.
[123] *Id.* at 60,362-363, 60,381.
[124] *Id*. at 60,361, 60,378.
[125] *See, e.g., id.* 60,409 (noting that the stated impacts of GUARD could change "significantly" if certain manufacturers are excluded "due to interactions with other CMS Innovation Center models or for any other reason.").
[126] 42 U.S.C. § 18114.

pricing into the U.S., along with the attendant policies that, as discussed below, have been soundly rejected in the U.S., would be certain to discourage innovation, leading to delayed breakthroughs and fewer products being available to U.S. patients.[127] This will be particularly detrimental to those living with rare diseases for which there is still no FDA-approved treatment, who already face deficits in care.[128] Moreover, it could potentially lead to drugs being removed from the U.S. market if the GUARD international reference penalty were sufficiently substantial to make continued U.S. commercialization of the drug economically infeasible.

Further, GUARD would undermine what has been a success story for U.S. health care—broad access to drug therapies in the U.S. has vastly improved health outcomes in this country.[129] It is not clear that new products developed overseas would continue to enter U.S. markets under the pricing regime GUARD would establish.

A look at patient access to drugs in many of the countries from which GUARD would derive reference pricing information is instructive. More than 100 medicines approved in the U.S. in the last decade are not available in European nations.[130] There is no reason to expect a different outcome in the U.S. as GUARD borrows European pricing. As such, GUARD would create unreasonable barriers to appropriate medical care, impede timely access to innovative drug therapies, and limit the availability of health care treatment to meet patients' full medical needs in violation of the "access to therapies" mandate of the Affordable Care Act.

E. GUARD Raises Issues Under the Part D Non-Interference Clause.

Section 1860D-11(i) of the Social Security Act bars the CMS from directing or controlling price negotiations between Part D plan sponsors and drug manufacturers, or from establishing drug prices under Part D.[131] By imposing externally-derived benchmarks and effectuating them through rebates, the economic structure of GUARD functions as price regulation. The Proposed Rule neither acknowledges the statutory non-interference constraint nor waives the potential restriction; and, as discussed above, CMS cannot invoke the authority of section 1115A to waive statutory requirements given that GUARD is not a model test.

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[127] *Fact Check: Weakening the Patent System Won't Lower Prices for Patients. It Would Undermine Medical Progress.*, COUNCIL FOR INNOVATION PROMOTION (Dec. 4, 2025), https://c4ip.org/fact-check-weakening-the-patent-system-wont-lower-prices-for-patients-it-would-undermine-medical-progress/.

[128] *FDA Rare Disease Innovation* Hub, U.S. Food & Drug Admin., https://www.fda.gov/industry/medical-products-rare-diseases-and-conditions/fda-rare-disease-innovation-hub (last updated Feb. 2, 2026).

[129] *See e.g.*, Bharath Krishnamurthy and Megha Parikh, *Drug Prices and Shortages Jeopardize Patient Access to Quality Hospital Care*, AM. HOSP. ASS'N (May 22, 2024), https://www.aha.org/news/blog/2024-05-22-drug-prices-and-shortages-jeopardize-patient-access-quality-hospital-care.

[130] *Putting Americans First: No Medicine is More Expensive Than the One Patients Can't Access*, BIO (Sept. 12, 2025), https://bio.news/bios-view/putting-americans-first-no-medicine-is-more-expensive-than-the-one-patients-cant-access/.

[131] 42 U.S.C. § 1395w-111(i).

VI. By Mandating the Importation of International Reference Pricing into the U.S. Without Addressing Patient Affordability, GUARD Would Undermine the Policy Goals of Innovation and Patient Access.

A. Imposing International Reference Pricing Will Undermine Incentives for Innovation and Threaten Existing Clinical Development Projects.

Any approach to incorporate government-set, arbitrarily lower prices into the U.S. reimbursement system risks reducing the incentives for investment in biotech innovation, driving capital to other, less risky investment areas, and reducing the pipeline of new transformational medicines. It is well established that the international arbitrary, government-set pricing levels that would be imposed under GUARD would have a deleterious impact on biotech innovation. These effects have been and would be seen both in terms of long-term impacts on investment in biotech innovation and near-term effects on the ongoing investment decisions made by biopharmaceutical manufacturers regarding ongoing clinical research and development.

First, and most importantly, biotech innovation plays a foundational role for improving patient care and health outcomes. Increases in life expectancy as well as significant reductions in morbidity are driven by and directly tied to biotech innovation. One longitudinal analysis, for instance, found that biotech innovation accounted for about two-thirds of the observed increase in mean age at death in the U.S. between 2006 and 2018.[132] At the same time, biotech innovation is an incredibly risky endeavor. Estimates suggest just 10–12% of drugs that reach human clinical trials succeed in clinical trials and become commercially available medicines.[133]

Economic analysis repeatedly confirms this point. In 2019, the Congressional Budget Office (CBO) evaluated a mandatory drug pricing proposal that relied on international reference pricing, capping drug reimbursement for certain products at 120% of other wealthy nations' pricing. The CBO estimated that the 2019 proposal would lead to approximately 8–15 fewer new drugs over the first decade after implementation and about 30 fewer over roughly 20 years, reflecting how reduced reimbursement is understood to reduce the amount of new medicines brought to market.[134] Such policy analyses are based on the robust economic evidence that reduced reimbursement for innovative biopharmaceuticals reduces the level of investment and therefore new products brought to market.[135]

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[132]Frank R. Lichtenberg, *The Effect of Pharmaceutical Innovation on Longevity*, HEALTH ECON. & BIOECON. L. Rev. (2022), https://pubmed.ncbi.nlm.nih.gov/35344806/.

[133]*Research and Development in the Pharmaceutical* Industry, CONG. BUDGET OFF., 5 (Apr. 8, 2021), https://www.cbo.gov/publication/57126 ("Only about 12 percent of drugs entering clinical trials are ultimately approved for introduction by the FDA.").

[134]*Re: Effects of Drug Price Negotiation Stemming from Title I of H.R. 3* CONG. BUDGET OFF. (Oct. 11, 2019), https://www.cbo.gov/system/files/2019-10/hr3ltr.pdf.

[135]*See*, *e.g.*, Carmelo Giaccotto, Rexford E. Santerre & John A. Vernon, *Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry*, 48 J. L. & ECON. 1 (2005).

The proposed international reference pricing approach would compound the significant damage already done to biotech innovation by the IRA's price-setting mechanisms. While CMS proposes to exclude from international reference pricing those products that have a Maximum Fair Price in place under the IRA, innovative products will be subject to punitive rebates in the first years after their launch, before they are eligible for selection under the IRA. Together, these two policies will compound each other's effects, introducing price setting to effectively the entire period in which a manufacturer expects to earn a return on investment.

The damage done by the IRA's price setting policies to incentives for research and development, particularly in relation to development of new indications, has already been substantial: Research by IQVIA found that if the IRA's price setting process had been in effect from 2000 to 2020, 33% of subsequent drug approvals for biologic therapies and 34% of subsequent drug approvals for small molecule therapies may not have been achieved.[136] Research by the National Pharmaceutical Council on the IRA's early impact found that, after the IRA's enactment, the percentage of drugs receiving a second orphan designation within 18 months of a first designation declined by about 48%, suggesting the law may be associated with reduced clinical development toward additional rare disease indications.[137]

Beyond the risk that importing arbitrarily low, government-set prices would pose to biotech innovation, adopting such measures in the U.S. would specifically undercut U.S. leadership in the biotechnology sector, at a time when such leadership is already under threat.

The United Kingdom is an instructive example of how national policy decisions to artificially de-value innovation can impact national biotech innovation and investment. While the UK was once ranked just behind the U.S. as a global leader in biopharmaceutical research and life sciences, it has seen a marked decline in foreign direct investment into its life sciences sector in recent years, which industry analysts have attributed to an increasingly uncompetitive pricing and reimbursement environment. According to the Association of the British Pharmaceutical Industry, life sciences foreign direct investment into the UK was around 58% lower in 2023 than it was in 2017, and the UK's global ranking for life sciences investment fell from second place in 2017 and 2021 to seventh in 2023.[138] This decline in investment has occurred alongside slowed growth in pharmaceutical R&D and a diminishing share of clinical trial activity in the UK, suggesting that pricing, access constraints, and relative reimbursement levels have begun to

[136] *Proliferation of Innovation Over Time: Frequency, Timing and Clinical Value of Expansions Post-Initial Approval* IQVIA INST. FOR HUM. DATA SCI. (Feb. 18, 2025), https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/proliferation-of-innovation-over-time.

[137] *Early Signals of the IRA on Orphan Drugs*, NAT'L PHARM. COUNCIL POLICY & EVIDENCE BRIEF 6 (May 2025), https://www.npcnow.org/sites/default/files/2025-05/FINAL%20NPC%20Orphan%20Policy%20Evidence%20Brief%20May%202025.pdf.

[138] *Creating the Conditions for Investment and Growth*, ABPI (Sep. 10, 2025), https://www.abpi.org.uk/publications/creating-the-conditions-for-investment-and-growth/.

undermine the country's appeal as a location for innovative drug development (as well as early product launches, a challenge discussed further below).[139]

Unfortunately, these same dynamics are now visible in the U.S. A June 2025 BIO survey found that more than a quarter of biotech investors are hesitant to fund early-stage research because drug-pricing policy has made future revenues unpredictable. Since 2021, the U.S. biotech sector has shed nearly 70,000 jobs. The proposed introduction of foreign reference pricing compounds the already unprecedented uncertainty and government involvement in pricing introduced by the IRA. The adverse impacts are likely to be particularly pronounced in the therapeutic areas targeting with GUARD, the same therapeutic areas identified as being high-need for Medicare enrollees and, in the case of GUARD, the same therapeutic areas that Congress itself took extra efforts to protect from access barriers. As discussed at greater length below, the costs of pricing uncertainty and importing price controls fall most heavily on small and mid-size firms, which historically have been the core of America's uniquely successful biotechnology economy.

B. GUARD Would Harm U.S. National Security by Undermining Biotechnology Leadership.

Challenging trends for the U.S. biotech industry—which international reference pricing would undoubtedly accelerate—are especially concerning at a time when U.S. leadership in biotechnology is especially under threat from China, posing risks to U.S. national security. China has already overtaken the U.S. in the number of registered clinical drug trials, with Chinese registered clinical trials totaling about 7,100 in 2024 compared with roughly 6,000 in the U.S., reflecting a shift in global clinical research activity toward China.[140] China has made clear commitments to bolstering its own biotechnology leadership—with *Made in China 2025* explicitly prioritizing biotechnology and biopharmaceuticals for a wide array of state supports.[141]

The Trump Administration has recognized the importance of biotechnology leadership to national security. For instance, Secretary Kennedy has underscored the role of biotechnology leadership in national security, noting in his budget testimony to Congress that the administration aims to" prioritize America's national security and competitiveness," recognizing that "[b]iomedical research continues to be one of our country's biggest exports."[142]

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[139]See, e.g., *Pharma Industry Says UK Pricing Revenue Unsustainable, Blocking Investments*, REUTERS (Mar. 20, 2025), https://www.reuters.com/business/healthcare-pharmaceuticals/pharma-industry-says-uk-pricing-revenue-unsustainable-blocking-investments-2025-03-20/.

[140]Adriel Bettelheim & Maya Goldman, *China Has Surpassed the U.S. in the Number of Drug Clinical Trials, With 1,100 More Trials Listed*, AXIOS (May 29, 2025), https://www.axios.com/2025/05/29/china-biotech-boom-us-drug-trials.

[141]Karen M. Sutter, *U.S.–China Competition in Emerging Technologies* 6 (U.S.–China Econ. & Sec. Rev. Comm'n 2024), https://www.uscc.gov/sites/default/files/2024-11/Chapter_3--U.S.-China_Competition_in_Emerging_Technologies.pdf.

[142]Sec'y Robert F. Kennedy, Jr., *Testimony on the President's Fiscal Year 2026 Budget Before the House Committee on Energy and Commerce, Subcommittee on Health* (June 24, 2025), https://www.hhs.gov/about/agencies/asl/testimony/2025/06/24/the-presidents-fiscal-year-2026-budget.html.

Industry observers have already noted that international reference pricing is a particularly risky and unwise policy in light of increasing competition from China.[143] While biotech manufacturers do typically generate revenue from their products worldwide, any manufacturer based in a large country—whether that be the U.S., China, or a large European country—will often generate a disproportionately outsized share of revenue from its home market. Should the U.S. choose the path of other wealthy nations, hobbling its biotech industry through dramatic pricing uncertainty and reimbursement cuts, the leadership of American biotech companies will be particularly threatened.

C. Imposing Foreign Reference Pricing Will Undercut American Patients' Access to Medicines and Worsen American Health Outcomes.

Most concerning from the perspective of Medicare beneficiaries today, GUARD would compel importing pricing frameworks that have repeatedly resulted in slower access, and in some cases no access, to innovative therapies. The evidence is clear that the pricing and reimbursement policies in many of the reference countries, such as peer European nations, Japan, Canada, and Australia, have significantly delayed or narrowed access to therapies.

It is important to underscore that the core concept of international reference pricing fails to recognize that prices in other countries can have significant effects on coverage and beneficiary access in such countries. Countries around the world routinely attempt to rely on arbitrarily low pricing, without consideration of potential impacts on access. Other nations' pricing mechanisms routinely disregard product innovation, including improvements that enhance the health, convenience and safety of the patient. Prices in many foreign nations are governed by payers with near monopolistic pricing power, setting the rules and acting as both judge and jury. The resulting prices do not recognize innovation and offer scant opportunities to seek appropriate value. In other nations, manufacturers are routinely faced with a moral dilemma when securing fair reimbursement for innovative medicines: accept price controls or fail to bring life-saving therapies to patients. International reference pricing exacerbates this situation by layering multiple monopolistic approaches to further depress pricing. GUARD would perpetuate these deficiencies in other countries' pricing approaches and bring them directly to the U.S., a country that has historically had a reimbursement system focused on patient access and innovation.

Empirical research has long found that lower expected biopharmaceutical reimbursement and reimbursement uncertainty, indicators of a government's failure to properly value innovation, are associated with launch delays and reduced availability. One economic analysis across 25 nations found that countries with stricter price regulation and lower expected prices experienced significantly longer delays in the launch of new drugs, even controlling for income

[143] *Trump Gives a Boost to China's Biotech Companies*, WALL ST. J. (Dec. 31, 2025), https://www.wsj.com/opinion/donald-trump-drug-price-controls-most-favored-nation-cms-joe-biden-ed43a287.

and market size.[144] Cross-national analyses confirm that the U.S. tends to see earlier and broader availability of new medicines than other wealthy markets—those markets that GUARD would rely on for pricing information. For instance, a RAND study comparing drug availability and launch timing found that new medicines are more likely to be launched first in the U.S. than peer wealthy nations and that the U.S. has a higher share of globally available new drugs than peer countries.[145] Specifically, more than half of new drugs studied were launched first in the U.S., with an average lag of about one year before launch in other major OECD markets including Australia, Canada, France, Germany, Italy, Japan, and the UK[146] Industry analysis specifically of European markets similarly documents that patients in many European countries face delayed or foregone access to innovative therapies, with greater challenges in more price-constrained markets.[147]

Cancer care, where biotech innovation has driven significant improvements in survival rates in recent decades, is a prime example of how other nations' approaches to pricing and reimbursement delay or narrow access to the latest therapies. In oncology specifically, international analyses find meaningful cross-country disparities in the availability and timeliness of new cancer medicines, with the U.S. frequently among the earliest launch markets.[148] For instance, of the 74 cancer drugs launched between 2011 and 2018, 95% are available in the U.S., compared with 74% in the UK and 49% in Japan.[149] A recent multi-country study of hospital access to innovative oncology medicines in Europe found average delays of roughly two years between European Medicines Agency authorization and real-world patient access.[150]

These differences in access have real-world impact on cancer patient outcomes, with internationally comparable survival estimates showing that the U.S. is at or near the top for several common cancers in cross-country datasets. In breast cancer, for example, the U.S. five-

[144]Patricia M. Danzon, Y. Richard Wang & Liang Wang, *The Impact of Price Regulation on the Launch Delay of New Drugs—Evidence from Twenty-Five Major Markets in the 1990s*, NAT'L BUREAU OF ECON. RSCH., Working Paper No. 9874 (2003), https://www.nber.org/system/files/working_papers/w9874/w9874.pdf.

[145]Andrew W. Mulcahy et al., *Comparing New Prescription Drug Availability and Launch Timing in the United States and Other OECD Countries*, RAND CORP. (2024), https://www.rand.org/pubs/research_reports/RRA788-4.html.

[146]*Id.*

[147]*Root Causes of Unavailability and Delay to Innovative Medicines* EUR. FED'N OF PHARM. INDUS. & ASS'NS (2025), https://www.efpia.eu/media/er5dshuq/cra-efpia-root-causes-of-unavailability-and-delay-final-2025-report-29-apr-2025-stc.pdf.

[148]*Significant Worldwide Disparities in Availability and Timeliness of New Cancer Drugs,* BMJ GLOB. HEALTH (summary) (2024), https://ecancer.org/en/news/25479-significant-worldwide-disparities-in-availability-and-timeliness-of-new-cancer-drugs.

[149]*Save Cures: Importing International Reference Pricing in the United States*, BIOTECH. INNOVATION ORG. (BIO), https://www.bio.org/save-cures.

[150]V. Vokó et al., *Differences in Time to Patient Access to Innovative Cancer Medicines in Europe*, EUR. J. HEALTH ECON. (2023), https://pubmed.ncbi.nlm.nih.gov/37864395/.

year net survival estimate is 90.2%, with other high-income comparators having lower rates, such as including Canada, Japan, Australia, and England.[151]

Importing prices from systems where products consistently launch later and or never launch at all risks replicating in the U.S. the same dynamics, particularly for fast-moving fields like oncology where timely access can save and extend patients' lives.

D. Foreign Reference Pricing Imports Arbitrary Practices That Discriminate Against the Elderly and Disabled.

Concerningly, GUARD would not only import pricing from other countries that undermine innovation and access, but also pricing approaches that rely on analytic frameworks the U.S. has repeatedly and expressly declined to adopt for ethical reasons.

Specifically, most of the reference countries specified in the Proposed Rule incorporate cost-effectiveness methodologies that use quality-adjusted life years (QALYs) or similar metrics when informing pricing and reimbursement decisions. By contrast, U.S. law has drawn a clear line against the use of comparative clinical effectiveness research in ways that assign lower value to the lives of certain populations, such as the elderly or the disabled. The IRA explicitly provides that "the Secretary shall not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an elderly, disabled, or terminally ill individual as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill."[152] CMS also may not use comparative clinical effectiveness research in the development of certain Medicare policies in a manner that devalues life extension for elderly, disabled, or terminally ill individuals.[153]

Yet many of the countries that would be reference countries under GUARD rely on QALY-based or QALY-informed health technology assessment frameworks[154]—effectively making Medicare policy partly reliant on such frameworks. Critics have noted that QALY-based approaches can systematically disadvantage the elderly and individuals with disabilities—an approach that the U.S. has consistently and explicitly rejected bringing into federal health care financing.[155] By tying U.S. payment levels to prices formed under such frameworks, GUARD risks reintroducing through the back door analytic approaches that Congress has specifically and frequently rejected.

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[151] *Breast Cancer Five-Year Survival Rate*, COMMONWEALTH FUND (June 5, 2020), https://www.commonwealthfund.org/international-health-policy-center/system-stats/breast-cancer-five-year-survival-rate.

[152] 42 U.S.C. § 1320f-3.

[153] 42 U.S.C. § 1320e-1.

[154] *Use of QALYs in Health Technology Assessment*, INT'L SOC'Y FOR PHARMACOECONOMICS & OUTCOMES RSCH. (ISPOR) (2021), https://www.ispor.org/docs/default-source/cti-meeting-21021-documents/3f952ab5-029e-4321-acce-dedad1ea99d0.pdf?sfvrsn=a4b9694c_0 (noting the use of such frameworks in reference countries France, Germany, Italy, and Spain).

[155] Peter J. Neumann & Joshua T. Cohen, *QALYs in 2018—Advantages and Concerns*, CTR. FOR THE EVALUATION OF VALUE & RISK IN HEALTH, TUFTS MED. CTR. (2019), https://cevr.tuftsmedicalcenter.org/news/2019/pipcreply.

E. Imposing Foreign Reference Pricing Will Decimate Small and Mid-Size Biotech Companies.

CMS explicitly recognizes the need to consider how GUARD may affect smaller biopharmaceutical manufacturers, soliciting comment on "adjustments to the [model] that could be considered" to minimize impacts on small entities, as well as "other factors that could be considered to mitigate the impact on small manufacturers."[156]

This comment solicitation illustrates a foundational flaw in the premise of GUARD's, in that it necessarily will result in negative downstream effects across the industry, including small companies. However, the comment solicitation does not capture the true extent of the harm. First, the comment solicitation fails to acknowledge the harm GUARD would cause to mid-sized companies. Second, the harm that GUARD would do to small biotechnology companies is much greater than CMS seems to recognize. International reference pricing would be a devastating blow to these smaller companies, which play a central role in driving biotech innovation.

The modern biotech innovation ecosystem is in large part driven by small and emerging biotechnology companies. Empirical analyses find that a majority of novel medicines trace their origins to early stage or startup biotechnology firms; one recent study reports that roughly 55% of new medicines originate in such companies.[157] Economic analysis of the industry finds that small biotech firms are central to biotech innovation, serving as the initial discovery engine before larger firms provide later-stage development and commercialization.[158] Further, smaller biotech firms represent a large share of the overall research and development ecosystem, with one estimate finding that 70% of all clinical trials are undertaken by emerging biotech companies.[159]

Examining the products potentially subject to GUARD by the size of their current manufacturers (as CMS does) understates the role of small firms: Even in cases where a product covered by Medicare is currently sold by a much larger pharmaceutical company, often the original research and development work was undertaken by a smaller company that is later acquired by a larger firm or out-licenses its product to the larger firm. But even if a product is commercialized by a larger firm, the revenues received by the larger firm selling the product—dictated by price-constrained markets and pharmaceutical reimbursement—have downstream consequences on the revenues or ability to raise capital for much smaller firms that are much more sensitive to uncertainty. Small- and medium-sized biotech firms typically operate with limited cash buffers and high capital intensity. One 2024 industry analysis found that approximately 39% of biotechnology companies had less than one year of operating cash on

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[156] 90 Fed. Reg. 60,415.

[157] *Where Do New Medicines Originate?* VITAL TRANSFORMATION (Mar. 22, 2023), https://vitaltransformation.com/wp-content/uploads/2023/03/Where-do-new-medicines-originate_FINAL-HS-BIO-approved-2023_03_22-v3.pdf.

[158] *See*, *e.g.*, Bo Carlsson et al., *Biotechnology Firms as "Explorers" in the Pharmaceutical Innovation System: Evidence for External Knowledge Sourcing*, 41 RES. POL'Y 924, 927–30 (2012) (showing that small biotech firms are key sources of early innovation that large pharmaceutical firms later integrate).

[159] *A Step Toward a Stronger Bioeconomy*, BIO (May 21, 2020), https://www.bio.org/gooddaybio-archive/step-toward-stronger-bioeconomy.

hand, underscoring their reliance on predictable financing conditions and future revenue expectations.[160]

Many of these firms are directly and particularly at risk from a disruptive, arbitrary reference pricing regime in part because they depend heavily on a single or small number of pipeline assets or approved commercial products. For small- and medium-size clinical-stage companies, a limited number of lead programs often underpin their ability to attract investment and sustain operations. For small- and medium-size commercial-stage companies, revenue from one or a small number of approved products frequently finances multiple ongoing research and development programs. Revenue reductions like those expected under GUARD will undermine the financial viability of companies with concentrated pipelines and commercial portfolios, threatening their ability to continue to develop innovative products. Small- and medium-sized biotech companies are also uniquely vulnerable to international reference pricing because they may be more limited in their ability to distribute and secure favorable reimbursement abroad, leaving them more reliant on expected U.S. revenues as a primary driver of investment decisions and revenue for reinvestment in research and development.

Finally, the pricing information CMS would rely on for rebates on the products of smaller biotech manufacturers is likely to be especially unreliable because pricing data from other nations will be more limited. Smaller firms often launch first in the U.S., as the world's largest biopharmaceutical market, and, in some cases, never launch in many other wealthy nations because of the cost of securing regulatory approvals, extending distribution, and securing appropriate reimbursement for their products. In some cases, products widely sold in the U.S. may only be sold in one or two reference countries, making such prices an unreliable and inappropriate basis for U.S. pricing.

F. CMS's Approach to Out-licensed Drugs Reflects a Fundamental Misunderstanding of How Small and Mid-Size Biotech Companies Operate in a Global Marketplace

i. For Out-Licensed Products, the Proposal Would Not Effectively Operate to Influence Pricing in Another Nations.

CMS's discussion of how it plans to treat products under GUARD where manufacturers do not control pricing outside the U.S.—or even potentially have any relationship with the ex-U.S. commercializing company—rests on significant misunderstanding of the role of such out-licensing arrangements in fueling biotech innovation. Failing to recognize and address these dynamics risks significantly undermining the entire theory of international reference pricing pursued by the Trump Administration.

In the GUARD's sister rule, GLOBE, CMS notes concern that, if manufacturers are exempt from GLOBE in cases where they do not control pricing on their products outside the U.S., firms might

[160] *More Than One-Third of Biotechs Have Under a Year of Cash Left, EY Finds*, BIOSPACE (June 18, 2025), https://www.biospace.com/business/more-than-one-third-of-biotechs-have-under-a-year-of-cash-left-ey-finds

"transfer[] responsibilities to other entities to avoid model participation," and discusses the general possibility that some manufacturers may lack responsibility for ex-U.S. sales.[161] This brief treatment both misunderstands the role of foreign out-licensing licensing arrangements and elides the significant challenge to an international reference pricing framework that these financing mechanisms represent.

Out-licensing agreements are not short-term tactical responses to national pricing policy. Especially for small- and medium-sized biotech firms, they are typically long-planned commercial strategies driven by the need to secure financing to bring a product through the lengthy and costly process of clinical research and development. Academic and industry analyses consistently recognize licensing revenue as a central financing mechanism for small and mid-size biopharma firms.[162] These agreements are often executed many years before regulatory approval, at stages when a company's priority is securing enough funding to complete clinical development and often no other sources of financing are available.

By design, out-licensing arrangements represent up-front cash flow for the manufacturer, not an ongoing pricing strategy. After such an agreement is struck, a manufacturer typically has no control over pricing outside the U.S., as well as no access to such pricing information. Out-licensing arrangements are often a lifeline for emerging biotechnology companies that must rely on these transactions to sustain operations and finance clinical programs.

While such out-licensing agreements are essential financing mechanisms for many biopharmaceutical products to reach the market, their structure has direct implications for the theoretical foundation of international reference pricing. As the President's Executive Order on Delivering Most-Favored-Nation Prescription Drug Prices to American Patients stated, the Administration's pharmaceutical pricing policies intend to address situations in which manufacturers "deeply discount their products to access foreign markets, and subsidize that decrease through enormously high prices in the United States."[163] Secretary Robert F. Kennedy Jr. has emphasized that the theory of the administration's pricing policies is that "[o]ther developed nations must pay more, so Americans can pay less, thus preserving the innovation pipeline."[164] CMS has stated that GUARD aims to reduce Medicare spending while "protecting innovation."[165] Together, these statements underscore that part of the administration's theory

[161]Global Benchmark for Efficient Drug Pricing (GLOBE) Model, 90 Fed. Reg. 60,274 (Dec. 23, 2025) (proposed to be codified at 42 C.F.R. pt. 513).

[162]Eungdo Kim et al., *Factors Affecting Outbound Open Innovation Performance in Bio-Pharmaceutical Industry—Focus on Out-Licensing Deals*, 13 SUSTAINABILITY 4122 (2021), https://doi.org/10.3390/su13084122; *Kelchtermans et al., Do Licensors Learn from Out-Licensing? Empirical Evidence From the Pharmaceutical Industry*, 112 TECHNOVATION 102405 (2022), https://www.sciencedirect.com/science/article/abs/pii/S0166497221001863.

[163]Sec. 5(i), Exec. Order 14297, Delivering Most-Favored-Nation Prescription Drug Pricing to American Patients, 90 Fed. Reg. 20,749 (May 15, 2025).

[164]Robert F. Kennedy Jr., *American Patients Pay More So Others Can Pay Less—That Stops Now*, FOX NEWS (May 17, 2025), https://www.foxnews.com/opinion/hhs-sec-robert-f-kennedy-jr-american-patients-pay-more-so-others-can-pay-less-stops-now.

[165]*CMS Proposes New Mandatory GUARD Model,* CTRS. FOR MEDICARE & MEDICAID SERVS. (Dec. 21, 2025), https://www.cms.gov/newsroom/press-releases/cms-proposes-new-mandatory-guard-model.

for GUARD is that impacts on funding for biotech innovation can be limited because pricing will rise in other countries.

But that mechanism presupposes that a manufacturer can adjust ex-U.S. pricing in response to U.S. policy. Where rights have been out-licensed, however, the U.S. sponsor typically lacks any legal authority and practical leverage over foreign list or net prices. In many cases, it does not even possess reliable visibility into a product's pricing. Under these conditions, the policy lever intended to induce foreign price movement simply cannot work as described and intended.

The result is that GUARD risks imposing U.S. price constraints without generating the corresponding foreign price responses that are central to its rationale. For drugs subject to out-licensing, the link between U.S. and ex-U.S. pricing is either highly attenuated or non-existent. Mandating reference pricing in this context simply concentrates financial pressure on the U.S. sponsor, including smaller innovators whose business models depend on early out-licensing to bring innovations to market.

ii. Different Licensing and Distribution Permutations Would Make Reporting Pricing on Out-Licensed Drugs Effectively Impossible.

While CMS recognizes that manufacturers besides the manufacturer in the U.S. may hold marketing or distribution rights in a given reference country or market, CMS expresses the belief that "manufacturers do have access to all sales made for the set of international analogs that correspond to a GUARD Model drug."[166] This belief presumes that the Model Participant Manufacturer is always the upstream licensor of ex-U.S. marketing and intellectual property rights.

However, the complex market for the various legal rights required to market pharmaceuticals is rarely so clean cut. CMS's brief consideration of whether a manufacturer "has access" to "all sales" of a product disregards the vast variety and complexity of the individual rights that various entities may hold over any particular product.

The IRA's inflation rebate program assigns rebate liability to the manufacturer who holds the labeler code for any individual product, which the proposal largely adopts. While the labeler code is generally, though not always, an appropriate indicator of the entity that holds the marketing rights granted by an FDA approval, it does not always correspond with the sole entity with control over the net pricing of the product. Those marketing rights may be licensed to another entity to co-market within the U.S. who may set prices for certain SKUs or enter into commercial arrangements with payers. The IP rights for a product may be held by either the original licensor, who then licenses those rights to other entities to pursue marketing authorization in the U.S. or abroad, or a licensee who uses them to pursue separate marketing authorizations or distribution rights. In any of these arrangements the manufacturer may have any number of relationships with other entities with marketing rights or that are otherwise able to set prices for the product either in the U.S. or any of the reference countries. The diversity in

[166] 90 Fed. Reg. 60,371.

licensing structures available to manufacturers results in instances in which a manufacturer may be unable to even communicate with a third party about its pricing or sales of an international analog in a given market.

As an example, there are instances in which the entity who holds the NDA or BLA for purposes of marketing in the U.S., and therefore likely also holds the labeler code that would make them subject to GUARD, is licensing the intellectual property for the product from a licensor with multiple relationships globally. In such instances, the U.S. NDA or BLA holder may make significant investments in the product, such as funding the clinical studies necessary for U.S. approval. However, if the IP holder licenses the ex-U.S. rights to a third-party company, the NDA or BLA holder (itself a licensee) may have no insight to the ex-U.S. pricing or sales data and may even be contractually prohibited from communicating with that entity by virtue of its agreement with the IP holder, or legally restricted based on the antitrust or competition laws in a given market. In such instances, GUARD would place significant risk on U.S. entities making considerable investments in the U.S. market for the benefit of American patients while being entirely unable to forecast the impact on their ability to recoup that investment.

iii. Contractual Constraints on Global Pricing Control and Data Access

As previously discussed, many products currently contemplated as GUARD drugs are subject to any number of licensing arrangements that may influence the pricing metrics referenced. In the example described above, the GUARD manufacturer would likely face significant barriers in controlling international prices, accessing the type of pricing data requested, and even communicating with the global entities with access to such pricing power and data. In such instances where the U.S. entity is the licensee of the of the global IP holder, they often are one of multiple licensees with rights to pursue marketing approval in limited geographies. As one of many licensees, the U.S. manufacturer does not in fact "have relationships with . . . other businesses" as suggested in the proposed rule because their sole relationship is with the licensor. There are a number of common contracting hurdles that would make access to ex-U.S. pricing impossible for the participating manufacturer:

- Typically, that license agreement would not expressly provide a right for the licensor to require the licensee to share pricing information;
- The U.S. licensee would have no privity of contract with any other global licensees, and licensees in ex-U.S. markets would have no incentive to reach any agreement with the participating manufacturer;
- Alignment on pricing between different licensees may be illegal under applicable competition laws; or
- The pricing information of a licensee is typically considered the confidential information of that licensee, and licensing agreements between the licensor and licensees likely include confidentiality provisions prohibiting the licensor from sharing the licensee's

confidential information, including pricing information (which, as noted above, is often not shared with the licensor in the first place).

These types of arrangements are complex, variable, and common, and the concerns above are limited to only one permutation of licensing scheme. These constraints currently exist for numerous products already on the market and are entirely ignored by GUARD.

iv. Global Competition and Confidentiality Laws Would Stand in the Way of Sharing Pricing Information for Out-Licensed Drugs.

In addition to the contractual hurdles associated with regulating pricing globally, various countries also maintain laws that would limit licensors and licensees from sharing sufficient information to implement GUARD's policy goals. Even if manufacturers could persuade licensor entities to draft contracts in a way that permits data sharing between licensees operating in different markets going forward, such data sharing may create risk under competition laws or binding confidentiality obligations imposed by ex-U.S. governments as a condition of reimbursement in various markets.

For instance, although list prices may be public, net prices for products subject to a public reimbursement scheme are generally considered confidential in the UK and in EU Member States. That is because pricing and reimbursement rules in some jurisdictions, including France and Germany, specify that negotiated net prices should remain confidential. For example, German Social Code (SGB V) § 130b provides that pharmaceutical companies and the GKV-Spitzenverband (GKV-SV), the central federal association of statutory health insurance funds in Germany, must maintain the confidentiality of the reimbursement prices they negotiate, unless otherwise provided by law. The French Social Security Code Article L.162-18 similarly requires that the Economic Committee for Health Products respects "trade secrecy" when setting or negotiating prices. Separately, drug products are subject to government contracting in most ex-U.S. jurisdictions, and these contracts will usually contain provisions protecting the confidentiality of net price information.

Similarly, most competition laws prohibit the exchange of competitively sensitive information, such as pricing information. Many ex-U.S. competition laws also prohibit resale price maintenance, such as where a manufacturer tries to set a minimum price at which its distributor sells its products. Taken together, these laws would make it very difficult, if not impossible, for a manufacturer to collaborate with ex-U.S. manufacturers and distributors of a GUARD drug in the way intended.

The combination of the actual or presumed confidentiality of net price information and competition law concerns means that companies will often have internal policies and procedures prohibiting or restricting the sharing of such information. Even where such policies do not exist, the potential compliance risks mean that they will be reluctant to share such information with unrelated companies, particularly those that are competitors.

v. GUARD Would Create New Barriers to Future Collaborative Marketing Arrangements Including Licensing Drugs into the U.S. Market.

While GUARD may create some incentive for manufacturers seeking to market products in the U.S. to pursue arrangements that would more easily allow for the disclosure of pricing information across markets, those same incentives are not present for other parties who may balk at sharing their pricing information with a U.S. licensee. As a result, the structure of GUARD risks making licensors less likely to seek to license their products in the U.S.

First, a manufacturer looking to license a product to market it outside the U.S. has no incentive to pursue an arrangement that would require it to disclose confidential pricing information, and, as discussed above, the U.S. manufacturer may not be a party to those negotiations.

Second, ex-U.S. manufacturers will still need to navigate the complex confidentiality and competition laws governing their ability to share pricing information. Those ex-U.S. manufacturers will be forced to take on compliance risk in their own markets, and the U.S. manufacturer would have minimal ability to provide any assistance in mitigating such risks because the U.S. manufacturer would have no way to ensure that an ex-U.S. government would not pursue enforcement action against its partner.

Third, creating the infrastructure to monitor and adjust prices globally in order to comply with U.S. policies will create additional costs that would need to be absorbed, likely through increased royalty payments from U.S. manufacturers forced to provide incentives for other global manufacturers. This will increase the cost of bringing innovative medicines into the U.S.

G. No Reliable, Consistent Pricing Sources Exist, Making the Pricing Inputs CMS Proposes to Use Unreliable and Inaccurate.

CMS's efforts to impose reference pricing faces the significant challenge that there is no single reliable, complete data source for the reference countries it proposes to use. This requires CMS to construct a complex, and therefore unpredictable, hierarchy of how it will use pricing from reference countries where there is only limited data for certain countries.

Even where pricing data exists and is public, however, CMS proposes to use an unreliable, unrepresentative concept. Under Method I, CMS would rely on publicly published prices from reference countries, citing to several publicly available databases. This pricing information, however, does not provide a reliable comparison for setting prices in the U.S.

List prices in other nations are not necessarily analogous to U.S. list prices, and they are not reliable indicators of either the actual list prices that matter in those markets or the prices ultimately paid. In other countries, the publicly reported price may be a formal ceiling, reimbursement benchmark, or reference figure used for regulatory purposes. As a result, the "publicly published" price may have no relationship to an economically meaningful transaction price in foreign markets. CMS does not, under this approach, analyze whether the published list prices it would use provide accurate reflections of market reality or whether they serve

primarily administrative purposes. Without some level of analysis regarding how other nations use and publish list prices, the use of these figures is not a sound basis for developing U.S. pricing policy.

Further, pricing information from reference countries in which "parallel trade" may occur—where a product is diverted from distribution in one country to another in order to obtain lower-cost products—can create situations where there are different prices for distributors in the same country wholly outside the control of the manufacturer, which are often more reflective of the pricing policies of the country in which the product was first placed into the flow of commerce. The existence of parallel trade as a relatively common practice,[167] especially in the EU where it is explicitly permitted under the common market,[168] makes potential reference pricing data even more unreliable.

H. GUARD Will Have Significant, Negative Impacts on Current and Future Rare Disease Treatments.

The federal government, including CMS, has an extensive existing policy structure intended to support innovation in treatments for rare diseases, or "orphan drugs," and yet CMS provides no discussion of how GUARD would affect access to and incentives for these products. This is especially concerning given the urgent need for more innovation and access in the area of rare disease treatments—approximately 10,000 rare diseases exist, and yet 95% have no FDA-approved treatment or cure.[169]

Orphan drugs, by definition, are therapies intended to treat rare diseases or conditions affecting small patient populations for whom the expected market return would otherwise be insufficient to justify development, and federal law has long recognized the necessity of special treatment for such therapies. In the U.S., this policy rationale was first codified in the Orphan Drug Act, which established financial incentives, grants, tax credits, and a seven-year exclusivity period for designated products.[170] The statute reflects Congress's express recognition that it is extremely difficult to finance treatments for rare diseases without targeted incentives. More recently, Congress expressly acknowledged the unique status of orphan drugs and eligibility rules that reflect the distinct dynamics of certain innovative therapies, as discussed above.[171] Congress has since strengthened these protections for orphan drugs through the ORPHAN Cures Act.[172]

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[167]EUR. FED'N OF PHARM. INDUS. & ASS'NS, *Key Data: The Pharmaceutical Industry in Figures* 4-5 (2024), https://www.efpia.eu/media/2rxdkn43/the-pharmaceutical-industry-in-figures-2024.pdf.

[168]*Remarks by Executive Vice-President Vestager on the Adoption of an Antitrust Decision Against Mondelēz for Cross-Border Trade Restrictions*, EUR. COMM'N (Mar. 22, 2024), https://ec.europa.eu/commission/presscorner/detail/en/speech_24_2784.

[169]*Rare Disease Drugs: FDA Has Steps Underway to Strengthen Coordination of Activities Supporting Drug Development*, GAO-25-106774, U.S. GOV'T ACCOUNTABILITY OFF. (Nov. 18, 2024), https://www.gao.gov/products/gao-25-106774.

[170]21 U.S.C. §§ 360aa–360ee.

[171]Inflation Reduction Act of 2022, Pub. L. No. 117-169, §§ 11001–11003.

[172]An Act to provide for reconciliation pursuant to title II of H. Con. Res. 14 (commonly known as the One Big Beautiful Bill Act), Pub. L. No. 119-21, § 71203 (2025) (amending 42 U.S.C. § 1320f-1(e)).

Other orphan drug exclusions exist in statute, including in the 340B Drug Pricing Program.[173] Beyond these statutory protections, the Trump Administration has undertaken several administrative initiatives at FDA, including the publication of new principles for evidence to spur rare disease development, that would be undermined by the failure of GUARD to account for the particular risks of rare disease development.[174]

Given this longstanding statutory backdrop and bipartisan policy consensus, it is notable that CMS did not even mention the Orphan Drug Act in its proposed rule and does not address how these unique orphan drug dynamics should be considered under GUARD. Failing to account for orphan drug incentives in broad pricing models such as GUARD risks undermining the policy framework that has supported rare-disease innovation for four decades. The small patient populations characteristic of orphan conditions inherently limit revenue potential, meaning that expected returns are especially sensitive to policy signals affecting pricing and coverage.

International experience illustrates the risks of importing pricing regimes that do not support robust access to and support for rare-disease therapies. The U.S. has historically approved a larger number of orphan drugs than peer jurisdictions, reflecting the robust incentives for bringing orphan drugs to market in the U.S. Studies comparing U.S. and European orphan-drug frameworks have found that the U.S. system has yielded more orphan designations and marketed products, with Europe often exhibiting slower uptake and narrower reimbursement.[175]

Reimbursement policy is a key driver of narrower access in these comparator countries—countries that GUARD would rely on for pricing information. Studies examining orphan-drug coverage decisions across European countries have documented that, even in situations where products receive regulatory approval, reimbursement can be challenging, often tied to strict cost-effectiveness thresholds and budget impact concerns.[176] By contrast, U.S. coverage in Medicare has generally enabled broad availability for rare disease therapies. Importing pricing regimes from other nations where orphan drug access is much narrower risks narrowing patient access in the U.S. and undermining the important incentives provided in the U.S. system to support rare-disease innovation.

Preserving incentives to develop orphan drugs is also critical for the U.S. to maintain its leadership in biomedical innovation. In recent years, China has implemented a comprehensive national strategy to become a leader in biomedical innovation—threatening the leadership of the U.S. According to a 2024 report from the non-partisan Information Technology and Innovation Foundation, China's investments in biotechnology resulted in the country's global

[173] 42 U.S.C. § 256b(e).

[174] *FDA Advances Rare Disease Drug Development with New Evidence Principles*, U.S. FOOD & DRUG ADMIN. (Sept. 3, 2025), https://www.fda.gov/news-events/press-announcements/fda-advances-rare-disease-drug-development-new-evidence-principles.

[175] *See*, *e.g.*, A. Joppi et al., Rare Diseases and Orphan Drugs: Access to Treatment in Europe, 13 EXPERT REV. PHARMACOECON. OUTCOMES RES. 497 (2013).

[176] *See*, *e.g.*, E. Picavet et al., Market Uptake of Orphan Drugs — A European Analysis, 7 ORPHANET J. RARE DISEASES 41 (2012).

share of value-added pharmaceutical output growing from 5.6% in 2002 to 24.2% in 2019.[177] Moreover, the number of clinical trials conducted in China has more than doubled from under 3,000 in 2017 to more than 7,000 in 2024.[178] Against this backdrop, China announced this January that it would, for the first time, grant orphan drugs seven years of market exclusivity.[179] The purpose of this exclusivity is to continue to foster and develop a vibrant biotechnology industry in China for rare disease therapies. Given this development, it is critical to preserve American competitiveness by ensuring that the incentives for developing orphan drugs remain robust. By applying the GUARD model to orphan drugs, CMS is undermining American competitiveness at a time when the country faces a clear threat to its leadership in biomedical innovation.

A further concern is that international reference–based pricing for orphan drugs is likely to be systematically less accurate and more distortionary than for traditional mass-market medicines because many peer countries are less likely to cover such products at all. When a drug is not broadly reimbursed in reference countries, prices that are gathered by or reported to CMS may reflect atypical circumstances, such one-off access programs, rather than a meaningful market price. In some cases, there may be no meaningful price information at all because the therapy is either not approved or effectively unavailable through national health systems, such that list price information is not published for a product in many countries. Finally, pricing comparisons across countries may also be unreliable in cases where, because a rare disease is genetically driven, countries have dramatically varying sizes of patient populations for a given rare disease product. Using very limited data, for products where countries are especially likely to delay, narrowly restrict, or decline reimbursement, is unlikely to produce a valid pricing metric for Medicare to use.

I. Imposing International Reference Pricing Will Undercut Innovation and Access in Certain Promising and Complex Therapy Areas.

i. GUARD Would Harm Innovation By Applying a One-Size-Fits-All Rebate Across All Therapies, Ignoring Efforts to Reward Innovation through Exclusivities and Designations.

GUARD also harms innovation by applying a one-size-fits-all international reference pricing rebate over a certain threshold irrespective of how innovative such products may be. This policy ignores both the statutorily created FDA exclusivity periods that reward research and innovation and ignore FDA standards such as Breakthrough Therapy, Fast Track, and Priority Review designations that identify products that make an especially significant contribution to patient care.

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[177]Sandra Barbosu, *How Innovative is China in Biotechnology?*, INFO. TECH. & INNOVATION FOUND, (Jul. 30, 2024), https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/.

[178]*Id*.

[179]*See* Steve Usdin, China's Orphan Drug, Exclusivity Could Bolster Market, Incentivize Development, BIOCENTURY (Jan. 28, 2026), https://www.biocentury.com/article/658209/china-s-orphan-drug-exclusivity-could-bolster-market-incentivize-development.

Congress deliberately created exclusivities within the Food, Drug, and Cosmetic Act to reward defined types of research and innovation that advance public health, protecting incentives that, through the importation of international pricing information without regard to length of exclusivity granted, GUARD would undermine.

Congress has created time-limited protection from certain forms of competition as a policy lever to support innovative drug development in various areas.[180] GUARD would ignore the protection these exclusivities are intended to provide, directly undermining the FDA framework created to support innovation.

Separately, Congress and FDA have created expedited programs specifically to distinguish therapies that represent especially dramatic clinical advances. By applying the same international reference pricing methodology across included drugs without regard to these designations, the models disregard a key, congressionally endorsed signal of clinical value. That disconnect risks reduced incentives for investment in the types of therapies federal law is designed to encourage.

For instance, Congress established the Breakthrough Therapy designation to speed development and review for drugs treating serious or life-threatening conditions when early evidence suggests a major advance. The statute directs FDA to grant the designation if the drug is for a serious or life-threatening disease or condition and "preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints."[181] In a similar vein, Congress also created the Fast Track designation, allowing sponsors to request the designation during development. And receive benefits such as more frequent FDA meetings and communications and "rolling review" of a marketing application, which can speed the overall review timeline.[182] FDA's Priority Review designation, established through the Prescription Drug User Fee Amendments program, similarly reflects the federal government's judgment about clinical importance and value to patients. Priority Review is reserved for a drug that, if approved, "would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition."[183] In certain cases, Congress has established a more formal framework for providing Priority Review, such as the Qualified Infectious Disease Products designation.[184] By

[180]New chemical entity exclusivity provides five years of protection for drugs containing active moieties never before approved. See 21 U.S.C. § 355(c)(3)(E)(ii); 21 U.S.C. § 355(j)(5)(F)(ii). Orphan drug exclusivity provides seven years of protection for drugs approved to treat rare diseases. See 21 U.S.C. § 360cc(a). Generating Antibiotic Incentives Now (GAIN) exclusivity adds five years to existing exclusivities for qualified infectious disease products. See 21 U.S.C. § 355f(a)–(b). Three-year clinical investigation exclusivity rewards sponsors that conduct new clinical studies for a new indication or dosage form. See 21 U.S.C. § 355(c)(3)(E)(iii); 21 U.S.C. § 355(j)(5)(F)(iii). Pediatric exclusivity adds six months to existing patent and regulatory protections when sponsors perform FDA-requested pediatric studies. 21 U.S.C. § 355a(b)–(c).

[181]21 U.S.C. § 356(a)(1)–(2).

[182]21 U.S.C. § 356(b).

[183]*Priority Review*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/priority-review.

[184]21 U.S.C. § 360n-1.

not accounting for whether a product has met these innovation-linked standards, GUARD risks undervaluing therapies that regulators and Congress have already identified as especially clinically or publicly important.

ii. Plasma-Derived Therapies Would Be Put at Risk by GUARD.

While CMS requested comments regarding plasma-derived therapies only for the Global Benchmark for Efficient Drug Pricing (GLOBE) proposed rule, plasma products are sometimes covered under Part D, and the risks that these reference pricing proposals would post to access to plasma-derived therapies applies in GUARD as well.

Plasma-derived therapies rely on uniquely fragile supply chains and labor-intensive collection and manufacturing processes that place these products at heightened risk of supply disruption. Unlike most small molecules or standard biologics that can be manufactured at scale and held in inventory, plasma-derived therapies depend on continuous, donor-dependent collection. The existing Part B inflation rebate program already recognizes this vulnerability by providing special adjustments for plasma-derived products.[185]

Applying international reference pricing to products with such significant supply risks would compound this existing fragility by imposing rebates based on non-comparable foreign markets that often have very different drug manufacturing ecosystems and reimbursement arrangements. While CMS notes that rebates could be reduced for plasma-derived products during shortages in a manner similar to current Part B inflation rebate adjustments, such an approach does not mitigate the underlying risk, it would only be applied after a shortage is already in effect. This risk is further exacerbated by internationally benchmarked rebate pressures. Under GUARD, producers facing unpredictable rebate obligations calibrated to foreign price levels may have incentives to shift capacity away from fragile plasma-derived lines, potentially undermining the availability of critical therapies for beneficiaries.

iii. Imposing International Reference Pricing Will Also Undermine the Rise of New, Individualized and Genetically Targeted Therapies.

The international reference pricing and rebate framework is also poorly suited to ongoing shifts in the biopharmaceutical industry and the rise of highly targeted, personalized therapeutics, such as genetically targeted therapies. Even when regulated as small-molecule drugs, many of these products are designed to influence gene expression, RNA signaling, or downstream protein production in ways that are biologically sophisticated and patient-specific. Their clinical value often derives from precise molecular targeting rather than broad population use. At the same time, many of these therapies are long-acting, with dosing intervals measured in months or even years, which fundamentally alters the revenue, utilization, and lifecycle patterns that underlie biopharmaceutical pricing models today. GUARD, which attempts to develop standardized international price comparisons, is not designed to account for the rise of increasingly individualized therapies.

[185] 42 C.F.R. § 427.302(b)(1).

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While the GUARD rebate model is not designed to account for potential changes in reimbursement that may support access to genetically targeted therapies, importing price controls from other nations where such products are likely to be slower to enter the market will also undermine this potentially transformative but still nascent and capital-intensive market segment. Imposing pricing policies that introduce additional unpredictability—particularly those tied to foreign price benchmarks—could dampen investment in areas where investments are especially high risk but may yield revolutionary new therapies.

VII. Conclusion

BIO appreciates the opportunity to provide feedback to CMS through this comment. For the reasons described herein, BIO urges CMS to withdraw the Proposed Rule. We look forward to collaborating with CMS on alternative policy initiatives to meet the Administration's goals of reducing global free-riding and promoting patient access to their therapies. Should you have any questions, please do not hesitate to contact us at 202-962-9200.

Sincerely,
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