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

May 24, 2023

The Honorable Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244–1850

RE: Small Biotech Exception (CMS-10844)

Dear Administrator Brooks-LaSure:

The Biotechnology Innovation Organization (BIO) appreciates the opportunity to comment on the proposed Information Collection Request (ICR) on the Small Biotech Exception (CMS-10844) issued by the Centers for Medicare & Medicaid Services (CMS) on April 24, 2023. Under the Inflation Reduction Act (IRA), a drug qualifies for the Small Biotech Exception from negotiation for initial price applicability years 2026, 2027, and 2028 if spending on the medicine comprises: (1) a small percentage of Medicare program spending, and (2) a significant proportional share of a company's Medicare business.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or prevent them in the first place. As a result, our members' novel therapeutics, vaccines, and diagnostics not only have improved health outcomes but also have reduced healthcare expenditures due to fewer physician office visits, hospitalizations, and surgical interventions. BIO membership includes biologics and vaccine manufacturers and developers that have worked closely with stakeholders across the spectrum, including the public health and patient advocacy communities, to support policies that help ensure access to innovative and life-saving medicines and vaccines for all individuals.

Small biotech manufacturers are at the forefront of America's innovation ecosystem. At BIO, we represent hundreds of biopharmaceutical manufacturers, with the vast majority of our members being small manufacturers who are working on some of the most important and cutting-edge scientific and medical research. Emerging biotech manufacturers are exceptionally productive, taking into account their lower market capitalization, and are responsible for nearly 80 percent of clinical drugs in the

pipeline. Many of these companies have yet to achieve a revenue stream and rely on private capital and outside investment to fund their clinical trials and research.

As we have noted in previous comments to the agency, ensuring that qualifying manufacturers benefit from the small biotech provisions in IRA is critical as America seeks to maintain its global competitiveness in this strategically important growth sector. Importantly, the Small Biotech Exception recognizes that small biotech manufacturers with a single product that represents the vast majority of their Medicare revenue will be disproportionately impacted by negotiation, which could have an immediate and tangible impact on the ability of such manufacturers to invest in future R&D – and in particular, in areas that predominantly affect the Medicare population.

We appreciate that, based on our previous comments submitted to the agency on March 27, 2023, that CMS made several technical changes to the ICR's Supporting Statement and related forms. However, we continue to have two overarching, significant concerns.

First, we are disappointed that CMS has still not provided clarity and predictability in critical areas, including: how or when the agency will notify manufacturers regarding its determination of whether a drug qualifies for the Small Biotech Exception; what information regarding the exception will be made available to manufacturers (including 2021 expenditure data) and what information will be made public; how CMS will evaluate submissions for the exception; and a dispute resolution process in the event an application for the exception is denied. We recommend that CMS provide this clarity as soon as possible.

Second, we are very concerned with CMS's proposed approach that a manufacturer should only apply for the Small Biotech Exception if it meets the test of a high spend drug under Sec. 1192(d)(1). As we have noted in previous comments to the Agency, predictability in implementation of the IRA is incredibly important for manufacturers – even more so for small companies. But right now, small manufacturers are still unable to make informed assumptions regarding their qualification for the Small Biotech Exception based on the parameters set out in the revised ICR. For example, while CMS has the necessary expenditure data to make this determination, manufacturers currently lack access to these data. Such certainty is critical as most small biotech manufacturers have only one or a limited number of products on the market. *Therefore, we continue to recommend that any company that believes its drug qualifies for the Small Biotech Exception under Sec. 1192 (d)(2) should be able to apply and be approved for this exception this year regardless of whether the drug meets the test of a high spend drug under Sec. 1192 (d)(1).* We believe the statute clearly envisions such an approach, as the exception in Sec. 1192 (d)(2)(A) exempts from the term "negotiation eligible drug" a "qualifying single source drug" that meets either the test in Sec. 1192 (d)(2)(A)(i) or Sec. 1192 (d)(2)(A)(ii), with no requirement that such drug has met the "high spend" criteria under Sec. 1192(d)(1).

Our more detailed comments follow.

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Submissions for Initial Price Applicability Year 2026. In the revised Small Biotech Exception ICR form and Supporting Statement, CMS continues to assert that the ICR applies to initial price applicability year 2026 only. With regard to a manufacturer's eligibility for the exception, the agency notes that (emphasis added), "Manufacturers who might benefit from submitting a Small Biotech Exception request for initial price applicability year 2026 are those manufacturers of a qualifying single source drug who believe that (1) the drug meets the criteria for the Small Biotech Exception as set forth in section 1192(d)(2) of the Act and as described in the Initial Negotiation Program Guidance and (2) absent such a request, the drug will be considered a negotiation-eligible drug for initial price applicability year 2026 based on the criteria and process specified in section 1192(d) of the Act and the Initial Negotiation Program Guidance." If – despite our concerns – CMS continues to restrict the Small Biotech Exception ICR to initial price applicability year 2026, and encourages only manufacturers whose drug meets the test of a "high spend drug" under Sec. 1192(d)(1) to apply for the exception, we note that the agency has not made publicly available the data on which it will rely with regard to total expenditures for the purposes of determining (1) eligibility for the Small Biotech Exception under Sec. 1192 (d)(2), or (2) whether a drug meets the test of a "high spend drug" under Sec. 1192 (d)(1). As such, it is impossible for small biotech manufacturers to make a reasonable inference regarding whether a submission is warranted in the current or future years on the basis of the requisite statutory thresholds. Therefore, we continue to recommend that any company that believes its drug qualifies for the Small Biotech Exception under Sec. 1192 (d)(2) should be able to apply and be approved for this exception this year regardless of whether the drug meets the test of a "high spend" drug under Sec. 1192 (d)(1). We believe the statute clearly envisions such an approach, as the exception in Sec. 1192 (d)(2)(A) exempts from the term "negotiation-eligible drug" a "qualifying single source drug" that meets either the test in Sec. 1192 (d)(2)(A)(i) or Sec. 1192 (d)(2)(A)(ii), with no requirement that such drug has met the "high spend" criteria under Sec. 1192(d)(1)(A).

Clarity on Data Source for 2021 Drug Spending and Availability of Data for Manufacturers. Following on the point above, CMS should clarify and provide access to the data source it will use for identifying 2021 total expenditures for the qualifying single source drug. We understand CMS is considering use of Prescription Drug Event (PDE) data for the purpose of identifying whether a drug qualifies for this exception; at the same time, however, the agency has stated that the Medicare drug spending dashboard data published at *cms.gov* is not being used for the IRA negotiation provisions. We strongly urge CMS to make available to manufacturers the 2021 expenditure data it will be using so that this data can be validated by manufacturers that may apply for the Small Biotech Exception. In support of such an approach, we note that CMS has separately committed within its draft guidance on the new Part D Manufacturer Discount Program (dated May 12, 2023) to providing transparency on its methodology for identifying manufacturers eligible for phased-in discounts under the new program: "Prior to releasing the revised HPMS Discount Program module, which we expect to do in late 2023, CMS will release additional information explaining the methodology CMS will use to identify manufacturers eligible for phase-ins."

Clarity on Process and CMS Response to Small Biotech Manufacturer. CMS should specify not only the timeline for when the submission of information by the small biotech manufacturer is due, but also the timeline for CMS review and response to the manufacturer – In situations where CMS grants the exception as well as situations where CMS does not. To promote certainty for small biotech manufacturers, CMS should commit to responding to each manufacturer as far in advance of September 1, 2023, as possible. In support of such an approach, we note that CMS has separately asserted within its draft guidance on the new Part D Manufacturer Discount Program (dated May 12, 2023) its intent "to provide manufacturers that submit and attest to the required ownership information by a certain date (to be announced later this year) with information regarding their eligibility for the phase-ins prior to the statutory deadline of March 1, 2024 to enter into a Discount Program agreement for 2025." Our additional process recommendations follow.

- *Clear Timelines. It is critical that CMS issue guidance and that companies have ample opportunity to review such guidance before a final decision is made.* We suggest the following as a timeline that would allow for appropriate transparency, clarity, and completion of the process in advance of the September 1, 2023, publication of drugs selected for negotiation:
    - Submission by small biotech manufacturers due June 10, 2023;
    - CMS response to small biotech company (affirmative or negative) due by June 30, 2023;
    - Small biotech company response to negative determination by July 20, 2023;
    - Final CMS response to small biotech company by August 10, 2023.

- *CMS Response and Justification for Decision.* CMS should provide clarity on the form and content of its expected response and notification to small biotech manufacturers applying for the exception, specifically whether the response will be by letter, email, or other form of official communication. Further, if CMS determines that it does not agree that a small biotech drug qualifies for the exception, CMS's response should outline in sufficient detail how such a determination was made, including on which expenditure data the agency relied and other information, as relevant, that led to a negative determination. Further, CMS should indicate if the rationale for the denial is restricted to initial price applicability year 2026 or all years for which the Small Biotech Exception applies.

- *Dispute Resolution.* CMS should provide a dispute resolution process where the manufacturer can respond to and appeal a negative determination by CMS. Specifically, the small biotech manufacturer should have the opportunity to provide additional data or information to the agency to support its application for the Small Biotech Exception.

- *Flexibility.* Given that this is a new program and process, and that only a limited number of small biotech manufacturers will be providing submissions to CMS, we recommend that the agency allow for a flexible approach. For example, if CMS determines that information submitted by the small biotech manufacturer is incomplete or unclear, we urge CMS to engage in a dialogue with the manufacturer to resolve any outstanding issues to complete their submission. Further, for the first year of the program, we encourage CMS to allow a small biotech manufacturer to

submit information after the information submission deadline, such as in good faith circumstances where a small biotech manufacturer may later realize that it should qualify for the exception. Moreover, we ask that CMS allows the HPMS form to include either text fields for additional comments, or to provide the ability for manufacturers to upload comments to support information they provide in the form. CMS says that they will not consider what it deems to be "incomplete submissions," the Agency should allow manufacturers the ability to provide comment or clarity on some of the fields in the HPMS form. The rigidity of the HPMS system harms manufacturer data submissions, and therefore there should be an option to allow for comments in this system using one of the two options above. In the event that the Agency allows a comment section, it should allow for meaningful comments and therefore be at least 1,000 characters.

- *One-time Qualification.* We request that manufacturers should not need to reapply in subsequent years if a drug has previously received the Small Biotech Exception and there is no material change in the manufacturer's circumstances. As an alternative, manufacturers could submit an attestation that nothing in their application has materially changed from the prior year and if there has been a material change the manufacturer could submit an updated form. In support of such an approach, we note that within the Supporting Statement for the draft Medicare Part D Manufacturer Discount Program Agreement Information Collection Request (CMS-10846), the agency confirms that "The MDP agreement automatically renews after the initial effective period, and CMS will determine specified manufacturers and specified small manufacturers only once at the start of the program. As such, the burden described above will be a one-time burden on manufacturers." We believe this approach would also decrease the administrative burden on CMS related to the review of requests pursuant to the Small Biotech Exception in future initial price applicability years.

- *Clear Definition of Acquired.* We recommend CMS include a definition for what it means to be "acquired" pursuant to Sec. 1192(d)(2)(B)(ii). CMS should consider defining an acquisition as the transfer of substantially all assets of the manufacturer. Further, CMS should specify whether the acquiring manufacturer meeting the definition of a specified manufacturer will be determined at the time of acquisition. If the acquisition results in a change in eligibility for the small biotech exemption, an updated form should be submitted.

Confidentiality of Proprietary Information, Publication of Drugs Qualifying for Small Biotech Exception. CMS should fully protect the confidentiality of all proprietary information submitted in relation to this ICR. At the same time, CMS should outline its approach for sharing with the public information regarding the small biotech drugs the agency determines qualify for the exception. Further, BIO recommends that CMS publish a summary list of the small biotech drugs and manufacturers that qualified. In support of such an approach, we note that CMS has separately committed within its draft guidance on the new Part D Manufacturer Discount Program (dated May 12, 2023) to "publish a list of manufacturers eligible for the phase-ins prior to the start of the Discount Program". Such information will similarly be important

for understanding the impact of this IRA provision and provide further certainty to small biotech manufacturers. We believe, however, that more detail on how or why a specific manufacturer's drug qualified as a small biotech drug should only be released if that manufacturer chooses to do so.

ICR Form – Certification. The language in the certification section appears to be overly broad – we recommend amending as follows: "I reviewed the submission and made a reasonable inquiry regarding its content. I understand the information contained in this submission is being provided to ~~and will be relied upon by CMS for Medicare reimbursement purposes, including to~~ determine whether the covered Part D drug of the Submitting Manufacturer qualifies for the Small Biotech Exception, as described in section 1192(d)(2) of the Social Security Act."

Technical Clarity on NDA/BLA Data in Small Biotech Form. BIO thanks the Agency for clarifying two key aspects of the small biotech exception form: the scope of the NDC-11s that manufacturers must include and additional clarity on members of a company's control group. BIO has identified one additional area for clarification under question 2b. This question states:

> ***Question 2b:*** *Please list all New Drug Applications (NDAs) held by the Submitting Manufacturer for any drug products with the active moiety listed in Question 2a, or all Biologics License Applications (BLAs) held by the Submitting Manufacturer for any biological products with the active ingredient listed in Question 2a, as applicable.*
>
Application Number (123456)	***Application Type (NDA; BLA)***	***Submission Number (123)***	***Approval Date (MM/DD/YYYY)***	***NDA/BLA holder***

> *Add a separate row for each additional NDA / BLA.*

Based on the plain text of the question, our understanding is that CMS is asking manufacturers to input information only for original NDAs and BLAs. However, there is ambiguity as to how a manufacturer should enter data in the "submission number" field. The form seems to state that CMS expects a submitting manufacturer to include a three-digit number; however, the field seems extraneous in light of the form requesting the NDA application number for original applications only (i.e., the number would always be 000). We request that CMS clarify what is intended to be captured in the "submission number" field or explain relevance in this context.

Thank you for your consideration of these comments. We look forward to ongoing dialogue with you on these and other issues of importance to small biotech drug manufacturers.

Sincerely,
/s/

Crystal Kuntz
SVP, Healthcare Policy & Research