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Centers for Medicare & Medicaid Services
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Massachusetts Biotechnology Council
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RE: Information Collection Request (ICR) Form for Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA) (CMS-10847, OMB 0938-NEW)

Dear Mr. Parham:

The Massachusetts Biotechnology Council (MassBio) appreciates the opportunity to submit comments on the Centers for Medicare & Medicaid Services (CMS) proposed information collection request (ICR) for the Negotiation Data Elements under Sections 11001 and 11002 of the Inflation Reduction Act (IRA).¹

MassBio represents the premier global life sciences and healthcare hub of Massachusetts, which has a vibrant biomedical research and development community that is a global leader for medical discovery and innovation. MassBio's 1,600+ member organizations are dedicated to preventing, treating, and curing diseases through transformative science and technology that brings value and hope to patients. MassBio's mission is to advance Massachusetts' leadership in the life sciences to grow the industry, add value to the healthcare system, and improve patient lives.

As described in our recent comments in response to CMS's initial guidance regarding the Medicare Drug Pricing Negotiation Program ("Negotiation Program"), MassBio is deeply concerned about the impact the Negotiation Program will have on the future development of innovative and life-saving therapies, as well as on the world-leading small and emerging biotech companies based in Massachusetts. Given the potential impact on innovation and thus on vulnerable patient access to life-saving therapies, we continue to urge CMS to adopt a "do no harm" approach in implementing this program that errs on the side of mitigating against the potential disincentives created by the program's framework, and that allows the agency to make corrections as needed to preserve innovation. To these ends, it is essential that the information CMS collects for purposes of the Negotiation Program fully captures the value of a given selected drug.

The IRA directs CMS, for purposes of negotiating the MFP of a selected drug, to consider certain "manufacturer-specific data," which includes, among other things, research and development (R&D) costs. As outlined in greater detail, below, MassBio urges CMS to broaden the definition of R&D costs to enable CMS to accurately assess the true scope of these costs in the innovation ecosystem.

The IRA also directs CMS to consider "evidence about therapeutic alternatives." This includes the extent to which the selected drug represents a therapeutic advance and the extent to which the selected drug and its therapeutic alternatives address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy. In the ICR Form, CMS provides only the most general

¹ 88 Fed. Reg. 16,983 (March 21, 2023).

of questions regarding each of these dimensions, which is unlikely to generate the type of information CMS needs to consider the therapeutic impact of a given selected drug, let alone compare that drug to any therapeutic alternatives. To improve the quality, utility, and clarity of the information to be collected, MassBio recommends that CMS:

- Make the process less burdensome for the public to submit information regarding the negotiation factors in section 1194(e)(2) of the Social Security Act;
- Solicit information regarding key pharmacological dimensions and patient-centered impact to better compare selected drugs to their therapeutic alternatives;
- Solicit information on the impact on rare disease and mental health in assessing the impact of a selected drug on specific populations, and take additional steps to ensure that quality-adjusted life year (QALY) data are excluded from consideration; and
- Broaden the definition of unmet need, with a lens specific to health equity, and consider whether a selected drug addresses an unmet need on an indication-specific basis.

I. To improve the quality and utility of the information collected for the Negotiation Program, CMS should redefine the R&D cost questions to better reflect the complexity of the innovation ecosystem.

As outlined in the ICR Form, CMS is collecting information regarding a combination of costs incurred by the Primary Manufacturer, defined as the manufacturer that owns the NDA or BLA for the selected drug, to include: basic pre-clinical research costs, post-investigational New Drug (IND) application costs, completed FDA-required phase IV trials, post-marketing trials, abandoned and failed drug costs, and all other R&D costs. We are concerned that CMS's proposed information collection overlooks certain investments critical to drug development.

First, by focusing solely on R&D expenditures made by the Primary Manufacturer, CMS's proposed definition overlooks contributions made by the Secondary Manufacturer and others. Drug development is often a collaborative process, involving investments by both small biotech companies and larger pharmaceutical companies. This can take the form of licensing arrangements, co-promotion agreements, and other arrangements. By looking only at the expenditures made by the manufacturer that holds the NDA/BLA, CMS is ignoring a large portion of R&D costs. We also note that his approach is not supported by the statute, which looks at research costs of the "manufacturer," a term that's defined quite broadly to refer to:

any entity which is engaged in—

(A) the production, preparation, propagation, compounding, conversion, or processing of prescription drug products, either directly or indirectly by extraction from substances of natural origin, or independently by means of chemical synthesis, or by a combination of extraction and chemical synthesis, or

(B) in the packaging, repackaging, labeling, relabeling, or distribution of prescription drug products.²

CMS should therefore collect information regarding R&D spend from across the innovation ecosystem. However—contrary to the approach outlined in the ICR Form—it should not be the responsibility of the Primary Manufacturer to collect this information from Secondary Manufacturers or others. Not only is

² Social Security Act (SSA) § 1191(c)(1) (referencing SSA § 1847A(c)(6)(A), which in turn references SSA § 1927(k)(5)).

there no statutory basis for this approach, Primary Manufacturers generally lack access to information regarding the business operations of other manufacturers, and requiring companies to share this sensitive information amongst themselves would add burden and create legal risk. CMS should instead use the ICR Form to solicit information regarding R&D costs from each manufacturer, including Secondary Manufacturers.

In addition, CMS's proposed definition for abandoned or failed drug costs suggests the agency will consider failed or abandoned product costs only for products with some relation to the selected drug at issue (i.e., same active moiety, active ingredient, mechanism of action and therapeutic class). Although these categories capture many of the costs incurred in the development of a given drug, MassBio urges CMS to clarify that it will also solicit information from manufacturers regarding R&D costs for abandoned and/or failed research *that is not attributable to any particular product* across a manufacturer's selected drugs. Developers often incur significant costs in the early stages of the pre-clinical discovery and development process that may not be tied to any particular product, but that were instrumental in moving the needle of scientific discovery forward and laying the groundwork for subsequent innovations that do lead to life-saving therapies. This aspect of R&D is a vital component to the larger process, and should be a material factor considered by the agency.

II. MassBio supports the solicitation of information from the public, in particular patients and providers, but recommends making the submission process less burdensome.

As noted above, the IRA requires CMS to consider certain data on alternative treatments to a selected drug as part of the Negotiation Program. While the statute does not specify where these data come from, CMS is proposing to allow for optional submission from Primary Manufacturers and the public. CMS also proposes to review existing literature, conduct internal analyses, and consult subject matter and clinical experts.

MassBio strongly supports the collection of information from both manufacturers and the public at large regarding the negotiation factors set forth in section 1194(e)(2) of the Social Security Act. The public, in particular patients and providers, have first-hand experience receiving, furnishing, and prescribing selected drugs and it is essential that CMS consider their views on the value of a selected drug and its therapeutic alternatives as part of the negotiation process.

However, we are concerned that requiring the public to register via the HPMS system in order to submit this information is likely to significantly increase the burden on the public of submitting this information, and may deter robust participation in this process. We therefore recommend that CMS allow the public to submit information either via a general email inbox or by using a simple online form that does not require pre-registration.

III. To better compare selected drugs to their therapeutic alternatives, CMS should solicit information regarding key pharmacological dimensions and patient-centered impact.

Question 41 of the ICR Form asks for information on the following with respect to a selected drug relative to existing therapeutic alternatives: therapeutic impact; therapeutic advance; differences in safety profile; and current costs. In terms of therapeutic impact, CMS is looking at health outcomes, surrogate endpoints, intermediate outcomes, patient-reported outcomes, and patient experience. CMS is requesting this information on an indication-specific basis, as applicable.

As a threshold matter, we note that MassBio supports CMS's proposal to collect this information on an indication-specific basis. Given that each drug has a unique set of indications, it is generally the case that the indications for a selected drug will not entirely overlap with the indications with any of its therapeutic alternatives. Moreover, a given selected drug may have a differential therapeutic impact across indications. However, it is essential that CMS consider as potential therapeutic alternatives only those products with the same on-label indications that are actually used in clinical practice as alternatives for that indication. This approach would help ensure that CMS is comparing apples to apples and considering only products and indications for which there are sufficient data. We also urge CMS to provide transparency regarding the therapeutic alternatives it is considering before soliciting information on whether those are the correct therapeutic alternatives, as well as how those therapeutic alternatives compare to the selected drug.

We further urge the Agency to provide further guidance to manufacturers and the public regarding the information CMS is collecting to assess whether a selected drug can be appropriately compared to any proposed therapeutic alternatives in terms of both therapeutic impact and advance. For one, CMS should solicit information that appropriately distinguishes the selected drug and any proposed therapeutic alternatives in terms of key pharmacological dimensions. For instance, CMS should solicit information on the extent to which a given therapy is uniquely suited to treat specific conditions. For example, small-molecule drugs, in particular, are able to effectively accomplish delivery across the "blood-brain barrier," which is essential for the treatment of many mental health conditions.

To aid its determination of therapeutic advance and comparative effectiveness, CMS should also solicit and prioritize information on the ability of a selected drug to assist patients with respect to other important patient-centered measures, including the ability of patients to function and be independent. This is particularly important for therapies that treat debilitating disorders, such as rare disease, for which improvements in function translate into enormous improvements to quality of life. We do not, however, believe that CMS should be comparing drugs to non-pharmacologic interventions, as both treatment types are often used in tandem and thus should not be subject to comparison as alternatives. Accordingly, MassBio supports that CMS has solicited information regarding only pharmacologic therapeutic alternatives, and urge CMS to retain this framework for future initial price applicability years beyond 2026.

IV. In assessing the impact of a selected drug on specific populations, CMS should specifically solicit information on the impact on rare disease and mental health, and should take additional steps to ensure that QALY data are excluded from consideration.

Question 42 of the ICR Form asks questions regarding what is known about the comparative effectiveness of a selected drug with respect to specific populations such as individuals with disabilities, the elderly, the terminally ill and children. It also asks if there are other specific populations not noted that should be considered, and what is known about comparative effectiveness of the selected drug with respect to these populations.

In collecting information on the impact of therapies on specific populations, CMS should specifically note that it is collecting comparative effectiveness information regarding issues specific to rare disease populations and individuals with mental illness. These are populations that generally lack access to adequate therapeutic options, and for whom the value of a new therapy is particularly critical. For instance, for rare disease, health utility and services research and data are limited given small populations

and specialized knowledge base, and where there is an on-label therapy for a rare disease, it is often either the first on-label therapeutic option, or the first such option to be approved in decades.

MassBio strongly supports CMS's efforts to exclude information that treats extending the life of individuals in these populations as of lower value, for example certain uses of QALYs, in the negotiation process. This policy aligns with prohibitions set forth in statute, and will help ensure that CMS is not evaluating the value of a given therapy in a manner that discredits its benefit to the neediest and most vulnerable populations. However, we are concerned that certain data sources that violate this prohibition in a discrete way, for example, by describing the research methodology without use of the term "QALY," or by including a QALY analysis as a component of the research methodology without disclosing as much may nonetheless be submitted to CMS. MassBio therefore recommends that CMS disclose to manufacturers, as part of the negotiation process, all evidence that was considered by CMS in developing the initial MFP offer. A manufacturer can then use that information to ensure that any such data that involves QALYs and other similarly problematic metrics—either directly or indirectly—are not included in the manufacturer's counteroffer.

V. CMS should broaden its definition of unmet need, with a lens specific to health equity, and consider whether a selected drug addresses an unmet need on an indication-specific basis.

Question 43 of the ICR Form asks questions regarding whether a given selected drug addresses unmet medical needs. CMS is proposing to define a drug or biologic that meets an unmet medical need as "[a] drug or biologic that treats a disease or condition in cases where very limited or no other treatment options exist...." The instructions and only question for this section focus solely on whether the selected drug and its therapeutic alternatives address an unmet need. MassBio is concerned this question will not provide CMS with the full picture of whether a product has addressed an unmet need.

First, the question fails to consider gaps in therapeutic options *at the time the product was launched*. The ICR Form should thus solicit specific information on the historical context surrounding the selected drug and its therapeutic alternatives in assessing whether the therapy addresses an unmet need.

Second, the question inquires about unmet need generally, and without express consideration of the various indications for the selected drug. CMS should also enhance the quality and utility of the information to be collected by expressly soliciting information as to whether a selected drug meets an unmet need on an indication-specific basis, as it proposes to do for other aspects of its information solicitation.

Third, by focusing solely on the availability of other treatment options, CMS's definition of "unmet medical need" is far too narrow. This narrow definition will serve only continue to disincentivize further biopharmaceutical innovation, especially in these critical areas of unmet need. We recommend that CMS instead look to the FDA's definition outlined in its "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics." Under the FDA guidance, "[a]n unmet medical need is a condition whose treatment or diagnosis is not addressed adequately by available therapy. An unmet medical need includes an immediate need for a defined population (i.e., to treat a serious condition with no or limited treatment) or a longer-term need for society (e.g., to address the development of resistance to antibacterial drugs)."

Relatedly, CMS should also solicit and prioritize information that views unmet medical needs through the lens of advancing health equity and reducing health disparities by improving access to care among any

underserved communities, including those with high unmet need such as rare disease. In this vein, CMS should solicit information and place greater weight on the ability of the selected drug to treat patients in underserved populations. For example, in the solicitation process, CMS can highlight information on drugs that are able to treat later stages of cancer, as these drugs will disproportionately benefit vulnerable patients from underserved communities who, because of access and related issues, are often diagnosed at later and more advanced stages of disease.

VI. Conclusion

MassBio thanks CMS for your consideration of our comments. As the IRA will have a significant impact across our diverse membership, we would appreciate the opportunity to meet with CMS to discuss these comments and other IRA-related issues of interest to our members.

Best regards,

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CEO & President
MassBio