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Mr. William N. Parham, III
Director, Paperwork Reduction Staff
Office of Strategic Operations and Regulatory Affairs
U.S. Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Agency Information Collection Activities: Proposed Collection; Comment Request, [Document Identifier CMS–10844]

Dear Mr. Parham:

The Pharmaceutical Care Management Association (PCMA) appreciates the opportunity to comment on the notice with comment period issued by the U.S. Centers for Medicare & Medicaid Services (CMS) titled: "Agency Information Collection Activities: Proposed Collection; Comment Request," as published in the *Federal Register* on January 24, 2023.[1] This Information Collect Request (ICR) is related to the Inflation Reduction Act's (IRA) drug negotiation provision. Under this ICR, CMS seeks to identify what pharmaceutical manufacturers may need to submit to justify an exception from being selected for negotiation due to being a "small biotech." CMS also issued further guidance on this exclusion in its March 15 initial program guidance, and directed feedback on that guidance document's provisions regarding the small biotech exception to this ICR process.[2] While PCMA will be commenting on the initial guidance separately for other provisions, we are including our full suite of comments on the small biotech drug exclusion in this letter, as encouraged by CMS.

PCMA is the national association representing America's pharmacy benefit managers (PBMs), which administer prescription drug plans and operate specialty pharmacies for more than 275 million Americans with health coverage through Fortune 500 companies, health insurers, labor unions, Medicare, Medicaid, the Federal Employees Health Benefits Program, and plans offered for sale on the Exchanges established by the Affordable Care Act. PBMs negotiate price concessions with manufacturers on their brand medications to improve the value of the Part D program. These price concessions reduce premiums for all beneficiaries and provide access to

[1] 88 Fed. Reg. 4184, January 24, 2023.
[2] CMS, "Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, and Solicitation of Comments." Available at https://www.cms.gov/files/document/medicare-drug-price-negotiation-program-initial-guidance.pdf. March 15, 2023.

preferred drugs with reduced cost sharing. Negotiated drugs under the IRA will be priced no higher than the prices PBMs are already able to negotiate. We have an interest in ensuring that manufacturers do not find loopholes in the CMS program, so that Part D plans and their contracted PBMs have certainty as we continue to negotiate on behalf of the program for drugs not selected by CMS.

Section 1192(d)(2) of the Social Security Act outlines the limited exception to drug selection for "small biotech drugs" available for price applicability years 2026, 2027, and 2028. Under the law, a manufacturer can request the exception on behalf of its drug if selected, if it is less than 1% of total Part B or Part D spending, as applicable, and 80% or greater of the manufacturer's total revenue under Part B or Part D, as applicable. The small biotech exception pairs with the low Medicare spend exception at the bottom of the list of negotiation eligible drugs. Under that exception (SSA Section 1193(e)(3), products with total sales under Part B and D combined of less than $200 million (adjusted each year for inflation) are not eligible for negotiation.

In evaluating the statute and guidance, we believe that the guidance's definitions leave CMS vulnerable to excluding drugs that a reasonable person would not categorize as "small biotech drugs." To protect the program, CMS should impose a very high burden of proof on each domain of the application. Further discussion follows below.

1. **The Exclusion as Implemented is Limited to Neither "Small" nor "Biotech" Drugs**

As a time-limited exception to negotiation under the new program, Congress may have intended to protect companies that relied upon a single drug for the lion's share of its revenue. The three-year period provides enough time for a manufacturer to adjust to the eventuality of a lower maximum fair price imposed upon it, though of course the drug would be beyond its initial period of exclusivity even during the time-limited exclusionary period. Congress gave this exclusion a peculiar name, however, since it neither excludes only "small" companies nor only "biotech" companies.

First, to qualify for the exclusion, a drug must have Medicare Part B or Part D revenue of less than 1% of program spending. In 2028, for example, this would mean less than $361 million in Part B spending, or less than $2.5 billion in Part D spending. The Small Business Administration (SBA) definition of a "small business" for pharmaceutical manufacturers is based on employee count, in part because many pharmaceutical manufacturers (in the R&D stage) may not have revenue. **We believe CMS should ask Congress to narrow the exception to actual "small businesses" based on a specific annual revenue threshold, aligned with Office of Management and Budget and SBA requirements.** Further, the law does not require that this revenue be a significant portion of the company's revenue. A given drug may not be a large fraction of Medicare Part D spending, for example, but may represent a significant portion of a company's total sales of a drug, if it is widely used in pediatric or other non-Medicare

populations.[3] This further erodes the public trust that only "small biotech" drugs are exempt from the negotiation process.

Second, "biotech drugs" as a general term means proteins like monoclonal antibodies and associated products produced using living cells, rather than "pharmaceuticals," which are chemically synthesized. However, most brand drugs covered by the Part D program (and thus most that will be eligible for negotiation) are pharmaceuticals, not biologics. Protecting relatively smaller businesses may be a valiant intent, but Congress has not designed a limited exclusion for **biologicals** here. The exclusion applies to any "qualifying single source drug," rather than narrowly to biologicals such as those licensed under Section 351(j) of the Federal Food, Drug, and Cosmetic Act, by contrast. **CMS should be prepared to answer questions about exclusions granted to non-biotech drugs.** Relabeling the exclusion through the PRA process and guidance could help clarify the intent and likely beneficiaries.

A third concern is how CMS would organize manufacturers regarding their applicants for this exemption. In the initial guidance released March 15, 2023, CMS describes accepting applications from the BLA or NDA holders only (the "primary manufacturer" as defined elsewhere in guidance) rather than any "secondary manufacturer." While "secondary manufacturer" is not defined this way, we are concerned that CMS will receive and have to accept for exemption applications for drugs whose BLA or NDA holder is a relatively smaller company (meeting the 1% / 80% thresholds), but actually marketed by much larger pharmaceutical companies. The agreements between these companies usually pay royalties to the license or application holder, while the sales revenue is recognized by the marketing entity. We do not believe these arrangements fit the spirit of a "small biotech" exemption. The smaller entity has in effect sold its interest in this product, even if it still holds the license or application itself. We urge CMS to consider the many varied ways that the pharmaceutical industry can organize its sales and marketing activities before finalizing the guidance's definitions. **In short, we recommend that CMS work with Food and Drug Administration (FDA), Internal Revenue Service (IRS), the Securities and Exchange Commission (SEC), and other relevant federal regulatory agencies to create a database of NDA and BLA holders under the single employer standard.**

2. PCMA Analysis of Potential "Small Biotech" Drugs Under Draft Guidance

CMS estimates in the Paperwork Reduction Act's documentation that approximately 10 manufacturers may apply for the exclusion. Through our analysis, we arrived at about double the number of potential applications for IPAY 2026, 2027, and 2028. Using the Medicare Parts B and D drug spending dashboards, for program year 2021, along with the FDA's Orange and Purple Books, we identified the applicable BLA or NDA license holder for each drug, and

[3] For example, there is a drug indicated for the treatment of cystic fibrosis, with about $6 billion in total US sales in 2021. Medicare revenue is less than 10% of the product's US sales. It is not eligible for negotiation until 2029, but were it eligible, it would be excluded as a small biotech drug.

assessed whether they may potentially be “small biotech drugs” per the current guidance. We also accounted for the numerous other exceptions and exclusions to being selected for negotiation, using other publicly available data, including from FDA on orphan drug designations and indications.

In our assessment, we do not believe any of the top 10 drugs likely to be selected for negotiation for 2026 should qualify as “small biotech drugs.” However, CMS will receive proprietary information submitted by manufacturers on several of the exclusion domains, beyond the publicly available data we relied upon, and thus, its results may differ. We did find 14 drugs otherwise eligible for selection in 2026, 2027, 2028 that may be eligible for this exclusion. We also found that it is unlikely that any Part B drugs will need to apply for the exclusion, given the statute’s and guidance’s direction about spending needing to be below 1% of “total expenditures under such part” creates a very low ceiling for Part B expenditures relative to Part D. (Only drugs with approximately $360 or less in expenditures under Part B are eligible for the exclusion.) This yields a counterintuitive result: Part D drugs with significantly higher expenditures (up to $2.2 to $2.5 billion) can qualify for the exclusion relative to Part B drugs at the same spending levels. CMS should consider a different methodology that allows for negotiation of similar revenue drugs, across the two Parts, instead.

Appendix Table 1 at the end of this document includes the complete results of our analysis. Appendix Table 2 lists examples of drugs that are either quintessentially “Small Biotech Drugs” or drugs that pose logical concerns for CMS to consider in finalizing the exclusion criteria.

Conclusion

We understand the level of effort that CMS is undertaking while standing up this new drug pricing negotiation regime. We hope CMS appreciates the discussion in this letter, from an interested industry stakeholder, as it looks to finalize key details. It is critical to the PBM industry that pharmaceutical manufacturers are not able to identify loopholes, and “save themselves” from direct negotiation. We hope our suggestions help CMS narrowly define the limited and narrow small biotech drug exclusion for 2026, 2027, and 2028. If you have any questions on these suggestions and recommendations, please do not hesitate to contact me directly at tdube@pcmanet.org.

Sincerely,

Tim Dube

Tim Dube
Vice President, Regulatory Affairs

Appendix Table 1: Spending Thresholds and Potentially Eligible Drugs[4]

Price Applicability Year	Part B Small Biotech Exception Estimates	Part D Small Biotech Exception Estimates
2026	• N/A (Part B drugs cannot be selected)	• There are 95 drugs below the small biotech spending ceiling ($2.2 billion), above the low revenue threshold ($200 million), and otherwise eligible[5] • 13 of these drugs are potentially excludable as "small biotech drugs" based on our assessment • About half of them pose significant logical questions for CMS. See appendix table 2 for a deidentified description of these drugs
2027	• N/A (Part B drugs cannot be selected)	• There are 8 additional drugs between the small biotech spending ceiling ($2.4 billion) and low revenue threshold ($210 million) • 2 of these drugs is potentially "small biotech drugs" based on our assessment, in line with the spirit of the exclusion
2028	• There are 7 negotiation-eligible drugs between the small biotech threshold ($361 million) and low revenue threshold ($217 million) • 1 drug is potentially a "small biotech drug" based on our assessment[6]	• There are 3 additional drugs between the small biotech spending ceiling ($2.5 billion) and low revenue threshold ($217 million) • None of these drugs are potentially "small biotech drugs" based on our assessment

[4] Source: Spending thresholds are per the Medicare Trustees Report, 2022, for each applicable year. For Part D, we adjusted for DIR to estimate gross covered prescription drug costs. The estimated number of negotiation-eligible drugs is based upon a 5% inflation adjustment to the initial low revenue threshold of $200 million for price applicability year 2026. We used the Orange and Purple Books to identify NDA and BLA holders, respectively, along with verifying single source status and the Part B and Part D drug spending dashboards for program year 2021 to rank drugs by expenditures.

[5] We have accounted for the low revenue drug exclusion, orphan drug exclusion, plasma-derived product exclusion, potential biosimilar launches by 2028, and presence of generic drugs by 2024 in this estimate.

[6] Because the Part B 1% maximum spending threshold is much lower than the Part D 1% threshold ($361 million compared to $2.5 billion), none of the Part B drugs eligible for the small biotech exclusion are likely to rank in the top 40 of total expenditures.

Appendix Table 2: Sample of Potentially-Excluded "Small Biotech Drugs" for 2026-2028

Row Number	Therapeutic Area	2021 Medicare Part D Gross Spending Range	2021 Ranking Range "But for" Small Biotech Exclusion	Is NDA/BLA Holder the Same as Marketing Entity?	Should it be Eligible for Exclusion?	Comments
1.	Immune disorders	>$1 billion	11-15	Yes	Yes	Although this manufacturer has several marketed products, this one accounts for about 90% of its Part D gross expenditures.
2.	Mental health	>$1 billion	11-15	Yes	Yes	Although this manufacturer has several marketed products, this one accounts for about 90% of its Part D gross expenditures.
3.	Central nervous system	$750 million - $1 billion	16-20	Yes	Yes	Neurocrine markets one other drug, Ogentys, approved in 2020, but it does not appear in the Part B or Part D spending data for 2021. This would seem to qualify for the small biotech exclusion for 2027, if it qualifies based on all other rankings in five years' time.
4.	Gastrointestinal conditions	$750 million - $1 billion	16-20	Yes	No	This manufacturer markets about a dozen brand name drugs sold in the Part D program. Though it accounts for about 80% of the company's Part D spending at the NDA level, the company also markets a high spending drug whose NDA is held by another company. Including this other NDA drops the percentage to 45-50%.
5.	Cardiovascular disease	$750 million - $1 billion	16-20	Yes	Yes	This product is the manufacturer's only currently marketed product that generates spending in the Part D program.
6.	Oncology	$500 million - $750 million	21-25	No	No	See row 4 above. This is the product marketed by the maker of that drug.

Row Number	Therapeutic Area	2021 Medicare Part D Gross Spending Range	2021 Ranking Range "But for" Small Biotech Exclusion	Is NDA/BLA Holder the Same as Marketing Entity?	Should it be Eligible for Exclusion?	Comments
						Excluding both drugs would be a significant advantage for the marketing entity.
7.	Opioids	$250 million - $500 million	31-35	Yes	No	This drug is a qualified single source drug only because FDA has declined to approve any generics for it, to help prevent diversion of addictive narcotics. CMS should consider an exception to the exclusion in cases like these.
8.	Diabetes	$250 million - $500 million	31-35	No	No	This product was sold to a different entity than the NDA holder as part of a negotiated merger. The marketing entity has more than $5 billion in other Part D product spending, actually accounting for 5-10% of its revenue. CMS should ensure it is fully investigating which company is ultimately responsible for marketing a product, similar to rows 4 and 6.
9.	Mental health	$250 million - $500 million	26-30	Yes	Yes	This product is the manufacturer's only currently marketed product that generates spending in the Part D program.
10.	Central nervous system	$250 million - $500 million	31-35	Yes	No	FDA has not approved any generics because the product's initial approval predates FDA's authority to accept ANDAs. As with row 9, CMS should consider exceptions when FDA policy prohibits generic competition.

Row Number	Therapeutic Area	2021 Medicare Part D Gross Spending Range	2021 Ranking Range "But for" Small Biotech Exclusion	Is NDA/BLA Holder the Same as Marketing Entity?	Should it be Eligible for Exclusion?	Comments
11.	Kidney disease	$250 million - $500 million	36-40	Yes	No	The manufacturer has several other low-spend Part D drugs and a number of generic drugs on the market. CMS should consider whether the exclusion should aid diversified companies like these.
12.	Cystic fibrosis	$250 million - $500 million	51-99	Yes	Yes	This product is one of five marketed biologics products for this condition, and none are biosimilars.
13.	Cardiovascular disease	<$250 million	51-99	Yes	Yes	This drug is the only marketed product for this manufacturer with Part D spending. It may fall off for not exceeding the inflation-adjusted low revenue threshold in 2027 or 2028.