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)

Under the authority in sections 11001 and 11002 of the Inflation Reduction Act of 2022 (P.L. 117-169), the Centers for Medicare & Medicaid Services (CMS) is implementing the Medicare Drug Price Negotiation Program ("the Negotiation Program"), codified in sections 1191 through 1198 of the Social Security Act ("the Act"). The Act establishes the Negotiation Program to negotiate a maximum fair price ("MFP"), defined at section 1191(c)(3) of the Act, for certain high expenditure, single source drugs covered under Medicare Part B and Part D ("selected drug").[1] For the first year of the Negotiation Program, CMS will select 10 Part D high expenditure, single source drugs for negotiation. The MFPs that are negotiated for these drugs will apply beginning in initial price applicability year 2026. The negotiation period for initial price applicability year 2026 begins October 1, 2023, or when the manufacturer of a selected drug enters into a Medicare Drug Price Negotiation Program Agreement with CMS, whichever is sooner. Section 1194(e) of the Act requires CMS to consider two sets of factors as the basis for determining the offer and counteroffer throughout the negotiation process: (1) certain data that must be submitted by the manufacturer of each drug selected for negotiation and (2) evidence about alternative treatments, as available, with respect to each selected drug and therapeutic alternative(s) for each selected drug.

In accordance with section 1193(a)(4) and section 1194(b)(2) of the Act, the manufacturer must submit, in a form and manner specified by CMS, information on the non-Federal average manufacturer price ("non-FAMP") for the selected drug as defined in 38 U.S.C. § 8126(h)(5) and information that CMS requires to carry out the negotiation process, including the factors outlined in section 1194(e)(1) of the Act, which, in conjunction with the available evidence on the factors outlined in section 1194(e)(2), will serve as the basis for offers and counteroffers. In addition, manufacturers and the public may submit information on the factors outlined in section 1194(e)(2) of the Act, which describe evidence about the selected drug and its therapeutic alternative(s).

For the purposes of this Information Collection Request (ICR), a selected drug for initial price applicability year 2026 is defined as a drug included on the selected drug list published by CMS by September 1, 2023. In section 1191(c)(1) of the Act, the statute adopts the definition of manufacturer established in section 1847A(c)(6)(A) of the Act. Section 1193(a)(1) of the Act establishes that CMS will negotiate an MFP with "the manufacturer" of the selected drug. To the extent that more than one entity meets the statutory definition of manufacturer for a selected drug for purposes of initial price applicability year 2026, CMS will designate the entity that holds the New Drug Application(s) (NDA(s)) / Biologics License Application(s) (BLA(s)) for the selected drug to be "the manufacturer" of the selected drug (hereinafter "Primary Manufacturer"). Likewise, for initial price applicability year 2026, CMS will refer to any other entity that meets the statutory definition of manufacturer for a drug product included on the selected drug list and that either (1) is listed as a manufacturer in an NDA or BLA for the selected drug or (2) markets

[1] Hereinafter, "drug" includes drugs and biologics pursuant to the definition of a "qualifying single source drug" at section 1192(e)(1) of the Act.

the selected drug pursuant to an agreement with the Primary Manufacturer as a "Secondary Manufacturer." Secondary Manufacturers would include any manufacturer of any authorized generics and any repackager or relabeler of the selected drug that meet these criteria.

CMS will collect certain data from the Primary Manufacturer, including information on non-FAMP and the data identified in section 1194(e)(1) of the Act, and will collect information on evidence about a selected drug and its therapeutic alternative(s) per section 1194(e)(2) of the Act from any interested party. This ICR Form serves as one of multiple ways that CMS will collect data per section 1194(e)(2) (see the supporting statement for further details).

Note: This ICR focuses on information required for selected drugs for initial price applicability year 2026.

General Instructions

Overview

The Primary Manufacturer of each selected drug must complete Sections A through H for each of its selected drug(s), which are specifically:

- A: Selected Drug Information,
- B: Non-FAMP Data Collection,
- C: Research and Development Costs and Recoupment,
- D: Current Unit Costs of Production and Distribution,
- E: Prior Federal Financial Support,
- F: Patents, Exclusivities, and Approvals,
- G: Market Data and Revenue and Sales Volume Data, and
- H: Certification of Submission of Sections A through G.

The Primary Manufacturer is responsible for aggregating and reporting all necessary data on its selected drug(s) from other parties, as applicable.

Section I ("Evidence on Alternative Treatments") collects available evidence on the selected drug and its therapeutic alternative(s), as applicable. **Any interested party, including but not limited to patients and consumers, Part D plan sponsors and Medicare Advantage organizations, Primary Manufacturers, manufacturers of therapeutic alternative(s) for a selected drug, hospitals and health care providers, wholesalers, pharmacies, researchers, and other members of the public, is permitted, but not required, to submit information for Section I.** Any interested party who submits evidence in Section I must complete Section J ("Certification of Submission of Section I for All Respondents") as well.

Submission Method

Primary Manufacturers will submit the information for Sections A through J via the CMS Health Plan Management System (CMS HPMS). Instructions for Primary Manufacturers to gain access to CMS HPMS to submit data related to Sections A through J will be available at:

https://www.cms.gov/Research-Statistics-Data-and-Systems/Computer-Data-and-Systems/HPMS/UserIDProcess.

All respondents who are not Primary Manufacturers will use a separate user-friendly web application to access the questions in Sections I and J. This application will be accessible from an entry point on CMS.gov, as well as on the publicly accessible CMS HPMS landing page at https://hpms.cms.gov. In order to access the questions in Sections I and J through the web link, the respondent must provide an email address. A confirmation email message from CMS will be sent to the respondent-provided email address and the respondent must follow the steps contained in the email message to obtain access to the questions in Sections I and J. Additional instructions to access this public web application will be forthcoming from CMS and made available on CMS.gov. Submissions may not be saved for work completed in progress.

Technical assistance for Primary Manufacturers and other interested parties will also be made available.

Additional Instructions

- The instructions in this section apply to all Sections A through J. If a term included in this ICR is also included and defined in the Medicare Drug Price Negotiation Program: Revised Memorandum, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 ("the revised guidance"), the term's definition in this ICR is the same as in the revised guidance.
- For Sections A through G of this form, the Primary Manufacturer must provide data **only with regard to the selected drug as identified** under section 1192 of the Act unless the specific instructions for a question state otherwise. If a Primary Manufacturer has more than one selected drug, the Primary Manufacturer is required to make a separate submission of the information required in Sections A through G of this ICR for each selected drug.
- Respond "not applicable" to any question in Sections A to G and I that does not apply to the selected drug (or therapeutic alternative, as applicable, in Section I).
- Certification is required for submissions. Section H includes the Certification of Submission of Sections A through G for Primary Manufacturers. Section J includes the Certification of Submission of Section I for all respondents.
- For Sections A through G of this form, CMS will pre-populate or the Primary Manufacturer must submit, as indicated in the section, the applicable data for all dosage forms and strengths of the selected drug, including for dosage forms and strengths that were sold, labeled, or packaged by a Secondary Manufacturer.
- For non-monetary numeric amounts, include up to three decimal places.
- Response formats are indicated within any charts included in Sections A through G and I (e.g., # to indicate a numerical response is required).
- If the instruction for a particular response field indicates no explanation is necessary and no voluntary explanation is being provided, please include "not applicable (N/A)" in the free response field.
- Primary Manufacturers must timely notify CMS if any of the information submitted changes after the initial submission of data.

Instructions for Reporting Monetary Amounts

- When calculating and reporting monetary values, the information must be determined using the methodologies described throughout the document and consistent with generally accepted accounting principles (GAAP), when applicable. Describe the policies and methodologies used in the calculations in the free response field for the relevant question, as well as an explanation of the standard used if it is inconsistent with GAAP.
- When calculating monetary values, assume at most an 8.1 percent annual cost of capital for purposes of applying an adjustment.[2] If a Primary Manufacturer uses a cost of capital adjustment below 8.1 percent, that amount must be used.
- Monetary amounts must be reported in United States dollars (USD) and include two decimal places (i.e., dollars and cents).
- When converting another currency to USD, use the exchange rate applicable at the time the costs were incurred. The Internal Revenue Service (IRS) website lists government and external sources where historical exchange rates can be found to the day.[3] If the exact date of a sale or conversion is not known, use the yearly average exchange rate for that currency for the year the costs were incurred.[4] In the free response field, report the amount, the currency, the exchange rate, and time period(s) used in this calculation.
- Do not count the same costs in multiple places unless the additional specific instructions for that question instruct you to do so.
- Do not include any costs that are unallowable under an applicable law or costs that are otherwise expressly excluded from this ICR.
- Do not make any adjustments for inflation to any dollar amounts reported. As applicable, in the free response field, specify the applicable time period for a specific question (e.g., calendar quarter, calendar year) and report the cost and revenue per each applicable time period. CMS will make the relevant inflation adjustments, as necessary.

A. Selected Drug Information

Primary Manufacturer Response Required

In Section A, for each selected drug for initial price applicability year 2026, CMS will populate the CMS HPMS with the list of the 11-digit National Drug Codes (NDC-11s) marketed by the Primary Manufacturer and any Secondary Manufacturer and published in accordance with section 30.4 of the revised guidance, meaning those NDC-11s of the selected drug that:

(1) had Part D PDE utilization in the 12-month period beginning June 1, 2022 and ending May 31, 2023, or
(2) which CMS believes are likely to have Part D PDE utilization in the future (for example, NDC-11s associated with recently approved NDAs / BLAs).

[2] Most studies on research and development (R&D) costs apply a cost-of-capital adjustment to each company's R&D spending to reflect the lag between investment and return on investment. The use of 8.1 percent is consistent with assumptions used by the Congressional Budget Office, see "Research and Development in the Pharmaceutical Industry," CBO (April 2021), available at https://www.cbo.gov/publication/57126.
[3] See: https://www.irs.gov/individuals/international-taxpayers/foreign-currency-and-currency-exchange-rates.
[4] See: https://www.irs.gov/individuals/international-taxpayers/yearly-average-currency-exchange-rates.

CMS will populate the CMS HPMS with the Dosage Form, Strength, Unit, and Labeler Code for each NDC-11 of the selected drug, including any NDC-11s that are marked as "discontinued". CMS will update this list as necessary (e.g., based on supplements from the Primary Manufacturer or other updates).

Instructions for Section A:

- Please indicate whether:
  (1) any NDC-11s associated with the NDA(s)/BLA(s) of the selected drug are missing from the list (e.g., because they are new NDC-11s, discontinued NDC-11s), including any missing NDC-11s of a Secondary Manufacturer of the selected drug,
  (2) any of the listed NDC-11s or additional NDC-11s are marketed or controlled solely by a manufacturer that is not the Primary Manufacturer or Secondary Manufacturer, and
  (3) any of the listed NDC-11s or additional NDC-11s have been discontinued.

Product Name	**NDC-11 Numbers**	**Marketed or Controlled Solely by a Manufacturer that is not the Primary or Secondary Manufacturer**	**Discontinued** *(Check box if discontinued)*	**Dosage Form (e.g., tablet)**	**Strength**	**Unit (e.g., mg)**	**Labeler Code**
Text to be pre-populated by CMS	*Numbers to be pre-populated by CMS*	*Yes/No*	*Check Box*	*Text*	#	*Text*	#

**Primary Manufacturer to add rows and identify any NDC-11s of the selected drug that are not pre-populated by CMS*

A Primary Manufacturer must report to CMS in writing any new NDC-11s of the selected drug at least 30 days prior to their first marketed date for any Primary Manufacturer or any Secondary Manufacturer(s) of such selected drug. The Primary Manufacturer also must report to CMS in writing the delisting of any NDC-11 of the selected drug that is no longer marketed by the Primary Manufacturer or any Secondary Manufacturer(s) within 30 days after its discontinuation.

B. Non-FAMP Data Collection

Primary Manufacturer Response Required

For Section B, the Primary Manufacturer is required to report the non-Federal average manufacturer price (non-FAMP) for its selected drug(s) for calendar year 2021 (or, in the case

that there is not an average non-FAMP available for such selected drug for calendar year 2021, for the first full year following the market entry for such drug).

CMS plans to use the reported NDC-11s, quarterly non-FAMP, and total package unit volume in the table below to calculate the average non-FAMP for calendar year 2021 for initial price applicability year 2026.

Definitions for Section B:

- Non-FAMP: Section 1194(c)(6) of the Act defines "average non-Federal average manufacturer price" as the average of the non-FAMP (as defined in 38 U.S.C. § 8126(h)(5)) for the four calendar quarters of the year involved.[5] For initial price applicability year 2026, these are the quarters of 2021. When there are less than 30 days of commercial sales data for all NDC-11s of the selected drug in calendar year 2021, the applicable year will be the first full calendar year following market entry of such drug. When there are at least 30 days of commercial sales data but less than a calendar quarter of data to calculate the non-FAMP in calendar year 2021 (or the first full year following market entry of such drug, when applicable) for a given NDC-11 of such drug, the non-FAMP reported by the manufacturer to CMS should reflect the temporary non-FAMP predicated upon the first 30 days of commercial sales data. The temporary non-FAMP should be calculated following the same methodology used to calculate the temporary non-FAMP amount used to determine the Temporary Federal Ceiling Price, as described in the Department of Veterans Affairs (VA) 2023 Updated Guidance for Calculation of Federal Ceiling Prices (FCPs) for New Drugs subject to Public Law 102-585. Any restatements of the non-FAMP made in any manufacturer non-FAMP submissions to the VA must be reflected in the non-FAMP submitted to CMS.
- Non-FAMP unit: Non-FAMP unit is the package unit as described in 38 U.S.C. § 8126(h)(6).
- Non-FAMP dosage form unit: The non-FAMP dosage form unit is the dosage form of the NDC that is reported in the "Dose form" field of the Excel workbook used by the Office of Pharmacy Benefits Management Services at the VA to collect non-FAMP information.

Instructions for Section B:

Please follow the instructions below when completing the following tables.

- Please complete the table immediately below about the non-FAMP for each calendar quarter of 2021 for the selected drug (or, in the case that there is not an average non-FAMP available for such drug for 2021, for calendar quarters for the first full year following the market entry for such drug).

[5] The term "non-Federal average manufacturer price" means, with respect to a covered drug and a period of time (as determined by the Secretary), the weighted average price of a single form and dosage unit of the drug that is paid by wholesalers in the United States to the manufacturer, taking into account any cash discounts or similar price reductions during that period, but not taking into account— (A) any prices paid by the Federal Government; or (B) any prices found by the Secretary to be merely nominal in amount. 38 U.S.C. § 8126(h)(5).

- Please report the non-FAMP and total package unit volume for each NDC-11 of the selected drug. If an NDC-11 was not marketed, sold, or distributed in a particular calendar quarter, enter the NDC-11 and quarter but enter "0" in the total package unit volume field and leave the non-FAMP field blank.
- Non-FAMP and total package unit volume information must be provided by the Primary Manufacturer for its own NDC-11s and the NDC-11s of any Secondary Manufacturer(s).
- Any restatements of the non-FAMP for the four calendar quarters of 2021 (or, in the case that there is not an average non-FAMP available for such drug for 2021, for calendar quarters for the first full year following the market entry for such drug) made in any manufacturer non-FAMP submissions to the VA must be reflected in the table below.
- Please indicate the total number of package units sold during the quarter and that are used in the calculation of the non-FAMP in the total package unit volume field.
- Please include the non-FAMP dosage form unit that will allow CMS to convert the package unit to the National Council for Prescription Drug Programs (NCPDP) unit, which is used for Part D prescription drug event (PDE) reporting, if the non-FAMP dosage form unit is different from the NCPDP unit.

NDC-11	Calendar Quarter	Total package unit volume	Dosage form unit	Non-FAMP
Text	*QQYYYY*	*#*	*Text*	*$*

If the reported non-FAMP is for a calendar year other than 2021, the market entry date must be provided in the free response field below. If necessary, describe assumptions, methodological steps, and other information needed to interpret reported non-FAMP prices. If no explanation is necessary, please include "not applicable (N/A)" in the free response field.

FIELD	RESPONSE FORMAT
Explanation of Non-FAMP Calculation	*Text (1,000-word limit)*

C. Research and Development (R&D) Costs and Recoupment

Primary Manufacturer Response Required

Section C contains five questions, related to different types of R&D costs incurred by the Primary Manufacturer, including acquisition costs. Each of these questions requires the Primary Manufacturer to report, as applicable: (1) dollar amounts for R&D costs, which must be reported in the numerical response field and (2) explanations of how those costs were calculated in the free response field. Section C also contains one question about the Primary Manufacturer's global and U.S. total lifetime net revenue for the selected drug. This question requires the Primary Manufacturer to report, as applicable: (1) the dollar amount for global, total lifetime net revenue, which must be reported in the numerical response field, (2) an explanation of how this amount was calculated in the free response field, (3) the dollar amount for U.S. lifetime net revenue, which must be reported in the numerical response field, and (4) an explanation of how this amount was calculated in the free response field.

Definitions for Section C:

R&D costs mean a combination of costs incurred by the Primary Manufacturer for all FDA-approved indications of a drug falling into the five categories below, and excluding the following: (a) prior Federal financial support (see Question 9 in Section E), (b) costs associated with applying for and receiving foreign approvals, and (c) costs associated with *ongoing* basic pre-clinical research, clinical trials, and pending approvals:

1. R&D: Acquisition Costs
2. R&D: Basic Pre-Clinical Research Costs
3. R&D: Post-Investigational New Drug (IND) Application Costs
4. R&D: Abandoned and Failed Drug Costs
5. R&D: All Other R&D Direct Costs

CMS is calculating recoupment of R&D costs using both the global and U.S. total lifetime net revenue for the selected drug:

6. Recoupment: Global and U.S. Total Lifetime Net Revenue for the Selected Drug

The definitions and associated time periods for these terms are included below.

CMS is collecting costs only on FDA-approved indications of the drug up to the date the selected drug appeared on the selected drug list for a price applicability year, unless otherwise specified.

Instructions for Section C:

Follow these instructions for Questions 1 through 6 when reporting R&D costs:

- For each dollar amount listed below, the Primary Manufacturer must report one dollar amount in the numerical response field and a thorough explanation of the values, including any calculations or conversions and any assumptions made.
- All costs in this Section C are for FDA-approved indications of the selected drug, unless otherwise specified. Do not report any costs for indications that are not labeled indications.
- All dollar figures submitted to CMS must be cash-outlay costs to the Primary Manufacturer. They must exclude any costs to entities that are not the Primary Manufacturer.
- Reported costs for Questions 1 through 5 must be mutually exclusive for each question; in other words, no costs must be counted in more than one section. Similarly, reported costs for Questions 1 through 5 must be collectively exhaustive for all R&D costs; in other words, all R&D costs that the Primary Manufacturer incurred for the selected drug must be accounted for in Questions 1 through 5.
- If the Primary Manufacturer received any prior Federal financial support, as defined in Section E, for any of the costs listed in Questions 2 through 5 below (e.g., Basic Research, Clinical Trials, etc.), deduct such funding from the final calculated numerical amount before answering the relevant question and note that deduction in the applicable free response field. CMS will be collecting additional information on federal funding in Questions 9, 10, and 11. Please reference Section E for instructions on reporting prior Federal financial support.

- If the Primary Manufacturer shared the expenses described in Questions 1 through 5 for any period of time or activity with any entity that is not the Primary Manufacturer, then the Primary Manufacturer must report only costs the Primary Manufacturer incurred. Report how shared expenses were allocated among the Primary Manufacturer and any other entity or entities in the free response field for the relevant question.
- Follow the instructions for Reporting Monetary Amounts, including those related to converting to USD if R&D costs occurred in other countries. While R&D may occur in other countries and those costs must be included and reported in USD, costs associated with applying for and receiving foreign approvals must not be included.

Question 1: Primary Manufacturer Acquisition Costs of the Selected Drug

Please provide the information below about acquisition costs incurred by the Primary Manufacturer for the selected drug, as described in more detail below.

Definitions for Question 1:

For the sole purpose of data collection under section 1194(e)(1)(A) of the Act, acquisition costs are defined as costs associated with the Primary Manufacturer's purchase from another entity of the rights to hold previously approved or future NDA(s) / BLA(s) of the selected drug.

Instructions for Question 1:

- First, report whether the Primary Manufacturer acquired the right to hold previously approved or future NDA(s) / BLA(s) of the selected drug from another manufacturer.
- If the response is No, please skip to Question 2.
- If the response is Yes, please report the total costs of the acquisition(s) of the NDA(s) / BLA(s) of the selected drug in the total acquisition costs for the selected drug field.
- In situations where the total acquisition costs of the approved or future NDA(s) / BLA(s) of the selected drug included costs other than for acquisition of the selected drug, please (1) report those costs in the total acquisition costs field and (2) provide a proportional allocation of the total acquisition costs for the selected drug in the total acquisition costs for the selected drug field. In the free response field, please provide an explanation of the allocation of total acquisition costs for the selected drug, as applicable. If this situation is not relevant, please leave the total acquisition costs for the selected drug field blank.

RESPONSE FORMAT
Yes/No

FIELD	**RESPONSE FORMAT**
Total Acquisition Costs	*$*
Total Acquisition Costs for the Selected Drug	*$*
Explanation of Allocation of Total Acquisition Costs for the Selected Drug	*Text (1,000-word limit)*

Question 2: Basic Pre-Clinical Research for All Approved Indications of the Selected Drug

Provide the following information about total R&D costs incurred by the Primary Manufacturer for all FDA-approved indications for the selected drug related to basic pre-clinical research, as described in more detail below.

Definitions for Question 2:

- Basic pre-clinical research costs are defined as all discovery and pre-clinical developmental costs incurred by the Primary Manufacturer with respect to the selected drug during the basic pre-clinical research period and are the sum of (1) direct research expenses and (2) the appropriate proportion of indirect research expenses (defined below).
- For each indication of the selected drug, the basic pre-clinical research period is defined as the date of initial discovery *or* the date the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug (whichever is later) to the day before the IND application for that indication of the selected drug went into effect.[6, 7] The basic pre-clinical research period may include both the initial research on the discovery of the selected drug and basic pre-clinical research related to new applications of the selected drug. If the length of the basic pre-clinical research period for the selected drug cannot be calculated, use 52 months ending the day before the first IND application went into effect. For example, if the selected drug had five IND applications that went into effect, use the date of the first IND application that went into effect as the end date for the 52 month period.[8]
- Direct research costs are costs that can be specifically attributed to the discovery and pre-clinical development of the selected drug. Direct research expenses could include personnel (compensation for investigators and staff) researching the selected drug, materials for conducting basic pre-clinical research, and the costs of in vivo and in vitro studies on the selected drug before an IND application went into effect.
- Indirect basic pre-clinical research costs and relevant general and administrative expenses are operating costs for basic pre-clinical research beyond the basic pre-clinical research

[6] CMS acknowledges that the exact date of initial discovery might not be known, but manufacturers must use their best estimate.

[7] For the purposes of identifying the date the Primary Manufacturer acquired the right to hold the potential NDA(s) / BLA(s) or NDA(s) / BLA(s) of the selected drug, use the earliest date of acquisition for any NDA / BLA of the selected drug.

[8] CMS believes that 52 months represents a solid average across studies. For example, one study reported that the preclinical phase takes 52 months on average. See DiMasi, J, Hansen, R, Grabowski, H. The price of innovation: new estimates of drug development costs. Journal of Health Economics. https://fds.duke.edu/db?attachment-25--1301-view-168. Another study estimated that the preclinical phase can take 31 months on average. See DiMasi, J, Grabowski, H, Hansen, R. Innovation in the pharmaceutical industry: New estimates of R&D costs, *Journal of Health Economics*, 2016, as cited by the Congressional Budget Office (CBO) in Research and Development in the Pharmaceutical Industry, April 2021, https://www.cbo.gov/publication/57126. Other estimates have found that the preclinical phase ranges from three to six years. See PhRMA, "Biopharmaceutical Research & Development: The Process Behind New Medicines," 2015, http://phrma-docs.phrma.org/sites/default/files/pdf/rd_brochure_022307.pdf.

costs for the selected drug, including administrative personnel and overhead costs (expenses for clinical facilities and equipment) that are shared across multiple potential drugs or biologics. To calculate the proportion of indirect costs, the Primary Manufacturer must use proportional allocation, whereby the same proportion of spending allocated for direct research on the selected drug is used to estimate the proportional spending for indirect research.[9, 10] For example, if the *direct* pre-clinical research costs spent on the selected drug were approximately 10 percent of a Primary Manufacturer's total *direct* basic pre-clinical research costs, then *indirect* costs should be allocated proportionally, then indirect costs should be allocated proportionally, thus for the selected drug they should be 10 percent of the total spending on *indirect* pre-clinical research costs during that time period.

Instructions for Question 2:

- The amount reported for basic pre-clinical research in the numerical response field for Question 2 must be the sum of (1) direct research expenses and (2) a proportion of indirect research expenses.
    - If the Primary Manufacturer acquired the right to hold the most recent NDA / BLA of the selected drug after the last IND application submitted to the FDA went into effect, please include "$0" for Question 2.
    - If there were basic pre-clinical research costs after the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug, the basic pre-clinical research costs must be reported in the numerical response field.
- In the free response field, list the direct research expenses and the indirect research expenses for the selected drug, the percentage of direct and indirect spending on the selected drug out of the total direct and indirect basic pre-clinical research costs, an explanation of the values used in the indirect cost calculation, and a list of the activities the Primary Manufacturer included in the direct research expenses and the indirect research expenses.
- In the free response field, identify the length of the basic pre-clinical research period, which runs from: the date of initial discovery *or* the date the Primary Manufacturer acquired the right to hold the first NDA / BLA of the selected drug, whichever is later, to the day before the last IND application for an FDA-approved indication of the selected drug went into effect.

FIELD	**RESPONSE FORMAT**
Basic Pre-Clinical Research Costs for All FDA-Approved Indications of the Selected Drug	*$*
Explanation of Basic Pre-Clinical Research for All-Approved Indications of the Selected Drug, Including Allocation and Apportionment Methods	*Text (2,500-word limit)*

[9] Wouters OJ, McKee M, Luyten J., Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA.* 2020;323(9):844–853. doi:10.1001/jama.2020.1166.
[10] Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL., *Methods for the Economic Evaluation of Health Care Programme*. 3rd ed. Oxford, UK: Oxford University Press, 2005, https://pure.york.ac.uk/portal/en/publications/methods-for-the-economic-evaluation-of-health-care-programme-third-edition(e43f24cd-099a-4d56-97e6-6524afaa37d1)/export.html.

Question 3: Post-IND Costs for All Approved Indications of the Selected Drug

Please provide the following information on the direct costs incurred by the Primary Manufacturer beginning on the day the IND went into effect for the first FDA-approved indication for the selected drug through the date when the last FDA-required post-marketing trial was completed for the selected drug. The Primary Manufacturer must report the direct costs for all completed post-marketing trials for all FDA-approved indications of the selected drug. *Do not report costs for indications that are not labeled indications.*

Definitions for Question 3:

- Post-IND costs are defined as all direct costs associated with dosing and preparing the selected drug for clinical trials and the selected drug's Phase I, Phase II, and Phase III clinical trials for each FDA-approved indication. Post-IND costs also include all direct costs associated with completed FDA-required, post-marketing trials that are conducted after the FDA has approved a product. Post-IND costs exclude FDA-required, post-marketing trials that were not completed.
- Direct post-IND costs are defined as Institutional Review Board (IRB) review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the dosing and Phase I, Phase II, and Phase III clinical trials during the post-IND period. Direct post-IND costs also include patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting the completed FDA-required, post-marketing trial.
- The post-IND period begins on the day the IND went into effect for the first FDA-approved indication for the selected drug through the date when the last FDA-required post-marketing trial was completed for the selected drug.

Instructions for Question 3:

- The amount reported in the numerical response field must include all direct costs associated with dosing and preparing the selected drug for clinical trials and the selected drug's Phase I, Phase II, and Phase III clinical trials for each FDA-approved indication.
    - If the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug after all NDA(s) / BLAs were approved by the FDA for a selected drug, do not include any costs for these trials in the numerical response field.
    - If the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug and there were additional post-IND costs that followed the acquisition and were incurred before the FDA approved the most recent FDA-approved indication, those costs may be reported in the numerical response field. For example, if a Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug during the Phase I trial for the most recent FDA-approved indication, it may report the costs of the trials that followed the acquisition in the numerical response field.
- In the numerical response field, report the direct costs for all completed, FDA-required post-marketing trials for all FDA-approved indications of the selected drug.

    - If the Primary Manufacturer acquired the right to hold the NDA(s) / BLA(s) of the selected drug after FDA-required post-marketing trials were completed or if no such post-marketing trials were completed for the selected drug, do not include any costs for these post-marketing trials in the numerical response field.
- The free response field must note if the selected drug received early approval (e.g., through the accelerated approval pathway) and the type of approval pathway. If the selected drug received accelerated approval, include the direct costs for any completed post-approval confirmatory studies in the numerical response field. Direct costs for any post-approval confirmatory studies that have not been completed should be reported in Question 5.
- The free response field must list the applicable direct costs included and any calculations or conversions that were done.
- The free response field must identify the length of the post-IND period used in the calculations.
- The free response field may include the post-IND cost associated with each FDA-approved indication and may break down those costs down further for each clinical trial phase, as well as each completed, FDA-required post-marketing trial.

FIELD	**RESPONSE FORMAT**
Post-IND Costs for Approved Indications of the Selected Drug	*$*
Explanation of Post-IND Costs for Approved Indications of the Selected Drug, Including the Allocation and Apportionment Methods	*Text (4,500-word limit)*

Question 4: Costs of Failed or Abandoned Products Related to the Selected Drug
The Primary Manufacturer may allocate a portion of the direct costs spent on basic pre-clinical research and clinical research for failed or abandoned products related to the selected drug.

Definitions for Question 4:

- Failed or abandoned product costs include a sum of the portion of direct *basic pre-clinical research* costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and a portion of direct *post-IND costs* for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.
- Failed or abandoned product costs include a portion of direct *basic pre-clinical research* costs on drugs with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials.
    - Direct research expenses are costs that can specifically be attributed to the discovery and pre-clinical development of the drug.
    - Direct research expenses include personnel (compensation for investigators and staff) researching the drug, materials for conducting basic pre-clinical research, and in vivo and in vitro studies on the drug.

- Failed or abandoned products costs include a portion of direct *post-IND costs* for drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.
    - Direct post-IND costs are costs that can specifically be attributed to the dosing and clinical trials for the drug.
    - Direct post-IND costs include IRB review and amendment costs, user fees, patient recruitment, per-patient costs, research and data collection costs, personnel, and facility costs that are directly related to conducting dosing and clinical trials for the drug.

Instructions for Question 4:

- In the numerical response field, only include costs that can be directly attributed to failed or abandoned product(s) with the same active moiety / active ingredient or mechanism of action *or* drugs in the same therapeutic class as the selected drug that did not achieve FDA approval.
- In the free response field, detail how these costs were determined, what portion of direct costs were included for basic pre-clinical research and clinical research costs, and how the allocation was done.

FIELD	**RESPONSE FORMAT**
Costs of Allowable Abandoned or Failed Products Related to the Selected Drug	*$*
Explanation of Costs on Allowable Abandoned or Failed Products Related to the Selected Drug, Including the Allocation and Apportionment Methods	*Text (2,500-word limit)*

Question 5: Direct Costs of Other R&D for the Selected Drug Not Accounted for Above
The Primary Manufacturer must report the dollar amount of direct costs it attributes to research and development that were not accounted for in Questions 1 through 4.

Definition for Question 5:

- Direct costs of other R&D for the selected drug are any other allowable costs that do not align with R&D definitions 1-4. For example, other R&D direct costs may include direct costs associated with conducting FDA-required post-marketing trials that were not completed. No additional definitions adopted.

Instructions for Question 5:

- In the numerical response field, report the direct costs of all other R&D for the selected drug.
- In the free response field, please individually report each "other R&D direct cost" for the selected drug and define how each individual "other R&D direct cost" was calculated.

FIELD	RESPONSE FORMAT
Costs of Other R&D for the Selected Drug Not Accounted for Above	*$*
Explanation of Costs of Other R&D for the Selected Drug Not Accounted for Above, Including the Allocation and Apportionment Methods	*Text (4,000-word limit)*

Question 6: Global and U.S. Total Lifetime Net Revenue for the Selected Drug

In order for CMS to consider the extent to which the Primary Manufacturer has recouped its research and development costs, the Primary Manufacturer must report the global, total lifetime net revenue for the selected drug from all countries, including the U.S., in which the selected drug was sold on or after the date of approval as determined by each country's drug regulatory agency. The Primary Manufacturer must also report the subset of U.S. lifetime net revenue for the selected drug sold to all U.S. entities following initial FDA approval. The definitions and instructions for this section are separated into two categories: (1) definitions and instructions for reporting global, including U.S. total lifetime net revenue for the selected drug and (2) definitions and instructions for reporting U.S. lifetime net revenue for the selected drug.

Definitions for Question 6: Global and U.S. Total Lifetime Net Revenue for the Selected Drug

CMS will use both the Primary Manufacturer's global and U.S. total lifetime net revenue for the selected drug to determine the extent to which the Primary Manufacturer has recouped R&D costs for the selected drug.

Definitions for Question 6a: Global, including U.S., Total Lifetime Net Revenue for the Selected Drug:

- Global, total lifetime net revenue for the selected drug is defined as the direct sales and payments from all other entities, minus the discounts, chargebacks, rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, other price concessions or similar benefits offered to any purchasers or any royalty payments or percentage payments in purchase contracts.
- Global, total lifetime net revenue period is defined as the date the drug or biologic was first sold anywhere globally through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- If global, total lifetime net revenue for the selected drug is not available through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year, calculate net revenue through the most recent quarter for which such data are available.

Instructions for Question 6a: Global, including U.S., Total Lifetime Net Revenue for the Selected Drug:

- In the numerical response field, report the global, total lifetime net revenue for the selected drug for the global, total lifetime net revenue period.
- Global, total lifetime net revenue for the selected drug must be in nominal USD and reported from the date the drug or biologic was first sold anywhere globally to the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- In the free response field, include any relevant currency conversions, report the date ranges for the global, total lifetime net revenue period, and explain how the final amount was calculated.

FIELD	**RESPONSE FORMAT**
Global, Total Lifetime Net Revenue for the Selected Drug	*$*
Explanation of Global, Total Lifetime Net Revenue for the Selected Drug	*Text (2,500-word limit)*

Definitions for Question 6b: U.S. Lifetime Net Revenue for the Selected Drug**:**

- U.S. lifetime net revenue for the selected drug is defined as the direct sales and payments from U.S. entities, minus the discounts, chargebacks, rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, other price concessions or similar benefits offered to any purchasers or any royalty payments or percentage payments in purchase contracts.
- U.S. lifetime net revenue period is defined as the date the drug or biologic was first sold in the U.S. through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- If U.S. lifetime net revenue for the selected drug is not available through the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year, calculate net revenue through the most recent quarter for which such data are available.

Instructions for Question 6b: U.S. Lifetime Net Revenue for the Selected Drug:

- In the numerical response field, report the U.S. lifetime net revenue for the selected drug for the U.S. lifetime net revenue period.
- U.S. lifetime net revenue for the selected drug must be in nominal USD and reported from the date the drug or biologic was first sold in the U.S. to the date of the publication of the selected drug list that includes the drug as a selected drug for an initial price applicability year.
- In the free response field, report the date ranges for the U.S. lifetime net revenue period, and explain how the final amount was calculated.

FIELD	RESPONSE FORMAT
U.S. Lifetime Net Revenue for the Selected Drug	*$*
Explanation of U.S. Lifetime Net Revenue for the Selected Drug	*Text (2,500-word limit)*

D. Current Unit Costs of Production and Distribution

Primary Manufacturer Response Required

Section D contains two questions on current unit costs of production and distribution for the selected drug. Question 7 is a table in which to report the average unit costs of production and distribution for all of the NDC-11s included in the selected drug. Question 8 provides a free response field for explaining the methodology for calculating the amount reported in Question 7.

Definitions for Section D:

- In accordance with section 1191(c)(6) of the Act, the term "unit" means, with respect to a drug or biological product, the lowest identifiable amount (such as a capsule or tablet, milligram of molecules, or grams) of the drug or biological product that is dispensed or furnished.
- Units must be reported in one of the three NCPDP Billing Unit Standards (BUS)[11]: each (EA), milliliter (ML), or gram (GM). The unit reported must be specified for each of the NDC-11s of the selected drug. Selections of EA, ML, or GM must be made as follows:
    - "EA" is used when the product is dispensed in discrete units. These products are not measured by volume or weight. The Billing Unit of "EA" is also used to address exceptions where "GM" and "ML" are not applicable. Examples of products defined as "EA" include, but are not limited to:
        - Tablets;
        - Capsules;
        - Suppositories;
        - Transdermal patches;
        - Non-filled syringes;
        - Tapes;
        - Devices/Digital Therapies;
        - Blister packs;
        - Oral powder packets;
        - Powder filled vials for injection;
        - Kits;[12] and
        - Unit-of-use packages of products other than injectables with a quantity less than one milliliter or gram should be billed as "one each," for

[11] See: https://standards.ncpdp.org/Billing-Unit-Request.aspx#:~:text=Billing%20Unit%20Requests,grams%22%20or%20%22milliliters.%22.

[12] Kits are defined as products that contain one of the following: (1) at least two distinct items with different billing units; (2) one product packaged with medicated or unmedicated swabs, wipes and/or cotton swabs/balls; or (3) meters packaged with test strips.

example, ointment in packets of less than 1 gram or eye drops in dropperettes that contain less than 1 ML.

- "ML" is used when a product is measured by its liquid volume. Examples of products defined as "ML" include, but are not limited to:
  - Liquid non-injectable products of 1 ML or greater;
  - Liquid injectable products in vials/ampules/syringes;
  - Reconstitutable non-injectable products at the final volume after reconstitution except when they are in powder packets; and
  - Inhalers (when labeled as milliliters on the product).
- "GM" is used when a product is measured by its weight. Examples of products defined as "GM" include, but are not limited to:
  - Creams (of 1 GM or greater);
  - Ointments (of 1 GM or greater); and
  - Inhalers (when labeled as GM on the product).[13]

- Costs of <u>production</u> are defined as all (direct and allocation of indirect) costs related to:
  - Purchase of raw ingredients, including intermediates, active pharmaceutical ingredients, excipients, and other bulk chemicals;
  - Formulation and preparation of the finished drug product;
  - Quality control and testing of the drug; and
  - Operating costs for personnel, facilities, transportation, importation (if any), and other expenses related to the preparation of the finished drug product for the selected drug.
- Costs of <u>distribution</u> are defined as all (direct and allocation of indirect) costs related to:
  - Packaging and packaging materials;
  - Labeling (e.g., the mechanical aspects of printing and affixing the approved label);
  - Shipping to any entity (e.g., distributor, wholesaler, retail or specialty pharmacy, physician office or hospital, etc.) that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer; and
  - Operating costs for facilities, transportation, and other expenses related to packaging, labeling, and shipping to any entity that acquires the drug from the Primary Manufacturer or any Secondary Manufacturer.
- Current unit costs of production and distribution of the selected drug are defined to include:
  - Units (and associated costs) marketed by the Primary Manufacturer and any Secondary Manufacturer(s);
  - Average unit costs during the 12-month period ending May 31, 2023 (for selected drugs for initial price applicability year);

[13] https://standards.ncpdp.org/Standards/media/pdf/BUS_fact_sheet.pdf. *Permission is hereby granted to any organization to copy and distribute this material as long as this copyright statement is included, the contents are not changed, and the copies are not sold.*

    - Only units (and associated costs) produced and distributed for U.S. sales; costs incurred outside of the U.S. are included, provided that they are incurred for the production or distribution of units produced and distributed for use in the U.S.;
    - Only costs incurred by the Primary Manufacturer and any Secondary Manufacturers; such costs may include payments to third parties (e.g., contractors) performing activities that qualify as production or distribution, as specified above; and
    - Allocated shared operating and other indirect costs (such as capitalized production facility costs, benefits, generalized and administrative costs, and overhead expenses) specific to each NDC-11 based on unit volume.
- Current unit costs of production and distribution of the selected drug are defined not to include:
    - R&D costs; and
    - Marketing costs.
- For the purposes of this form, "marketing costs" are defined as expenditures incurred in the introduction or delivery for introduction into interstate commerce of a drug product, specifically including media advertisements, direct-to-consumer promotional incentives including patient assistance programs, promotion of the drug to health professionals, and other paid promotion.

Instructions for Section D:

Follow the instructions below when answering Questions 7 and 8:

- Production and distribution unit costs must be reported separately for each NDC-11 of the selected drug, including any NDC-11 of the selected drug marketed by a Secondary Manufacturer.
- Unit costs reported must represent the average per unit cost (1) within the time period specified below, (2) across all package types, and (3) calculated according to the instructions and using the definitions specified below.
- Use the response field in Question 8 to explain any shared operating and other indirect costs that were included in the response to Question 7.

Question 7: Per Unit Production and Distribution Costs

Please complete the following table using additional rows as necessary for the 12-month period ending May 31, 2023.

NDC-11	Average Per Unit Production Cost	Average Per Unit Distribution Costs	Indicate Unit Used	Total Unit Volume
12345-6789-01	*$XX.XX*	*$XX.XX*	*Select one:* • *Gram (GM)* • *Milliliter (ML)* • *Each (EA)*	#

Question 8: Explanation of Calculation of Per Unit Production and Distribution Costs

Please describe the methodology used to calculate the average per unit costs of production and distribution reported in Question 7, including which indirect costs were included, specific allocation methodologies, assumptions, and whether such assumptions apply to all or a subset of the data reported.

Specifically, include any assumptions about costs including, but not limited to:

- Allocated general and administrative overhead;
- Cost of capital;
- Labor compensation;
- Any included costs that were incurred outside of the U.S.;
- Allocated shared facility costs;
- Allocated shared transportation or other operational costs;
- Depreciation of facilities, equipment, or other assets involved in the production and distribution of the selected drug; and
- Number of units of drug samples and how their cost was determined.

FIELD	RESPONSE FORMAT
Explanation of Unit Production and Distribution Costs	*Text (2,500-word limit)*

E. Prior Federal Financial Support

Primary Manufacturer Response Required

Section E focuses on capturing prior Federal financial support for novel therapeutic discovery and development with respect to the selected drug.

Definitions for Section E:

- "Federal financial support for novel therapeutic discovery and development" refers to tax credits, direct financial support, grants or contracts, and any other funds provided by the federal government that support discovery, research, and/or development related to the selected drug.
- "*Prior* Federal financial support" refers to Federal financial support for novel therapeutic discovery and development (as defined above) issued during the time period from when initial research began (as defined above in the R&D Costs subsection), or when the drug was acquired by the Primary Manufacturer, whichever is later, to the day through the date the most recent NDA / BLA was approved for the selected drug.

Instructions for Section E:

Follow the instructions below when answering Questions 9, 10, and 11.

- When completing this section:

- Include all prior Federal financial support provided by federal agencies or Federally supported grants or contracts contributed to direct costs for the basic pre-clinical research and clinical trials phase of research and development for FDA-approved indications of the selected drug to the Primary Manufacturer only (do not include Federal financial support provided to applicable Secondary Manufacturers of a selected drug). These direct costs are costs that can be specifically attributed to the discovery, pre-clinical development, and clinical trials of FDA-approved indications of the selected drug. Please include prior Federal financial support that contributed to pre-IND and post-IND direct costs.
- Include prior Federal financial support received for indirect costs of developing the selected drug. These indirect costs are operating costs such as administrative personnel and overhead costs (expenses for clinical facilities and equipment) that are shared across multiple potential drugs or biologics.
    - To calculate the proportion of indirect costs, the Primary Manufacturer must use proportional allocation, whereby the same proportion of spending allocated for direct research on the selected drug is used to estimate the proportional spending for indirect research.[14, 15] For example, if the *direct* costs spent on the selected drug were approximately 10 percent of a Primary Manufacturer's total *direct* basic pre-clinical research costs, then *indirect* costs must be allocated proportionally, thus for the selected drug they must be 10 percent of the total spending on *indirect* costs during that time period.
    - For grants, Primary Manufacturers should use the indirect cost rate at the time of data submission to calculate the proportion of funds that should be allocated to indirect costs. This indirect cost rate could be the fixed rate, provisional/final rate, or predetermined rate.
- If the Primary Manufacturer received prior Federal financial support for a failed or abandoned product with the same active moiety / active ingredient or mechanism of action as the selected drug that did not make it to clinical trials and/or drugs in the same therapeutic class as the selected drug that did not achieve FDA approval, including indications for the selected drug that did not receive approval, the Primary Manufacturer should not include this amount in its answer for Question 9. Instead, the Primary Manufacturer must include this amount as a separate quantity when explaining prior Federal financial support in Question 10.
- If the Primary Manufacturer shared the prior Federal financial support described in Questions 9 through 11 for any period of time or activity with any entity that is not the Primary Manufacturer, then the Primary Manufacturer must report only costs the Primary Manufacturer incurred. Expenses should be allocated across entities based on each entity's respective stake in the selected drug's discovery and

[14] Wouters OJ, McKee M, Luyten J., Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018. *JAMA.* 2020;323(9):844–853. doi:10.1001/jama.2020.1166.
[15] Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL., *Methods for the Economic Evaluation of Health Care Programme*. 3rd ed. Oxford, UK: Oxford University Press, 2005, https://pure.york.ac.uk/portal/en/publications/methods-for-the-economic-evaluation-of-health-care-programme-third-edition(e43f24cd-099a-4d56-97e6-6524afaa37d1)/export.html.

development. The allocation to the Primary Manufacturer should be reported as a dollar amount and the percentage of the total amount allocated to the Primary Manufacturer should be included in the free response field in Question 10. For example, if the Primary Manufacturer was allocated 80 percent of the prior Federal financial support for a period of the selected drug's development, the Primary Manufacturer would include 80 percent of that support in its total number for prior Federal financial support in Question 9. Then, it would note the source of the shared prior Federal financial support and that that it received 80 percent of that support in Question 10. If the shared support came in the form of an agreement, the Primary Manufacturer would include this in the "Nature of Agreement" section of Question 11.

Question 9: Federal Funding Support Amount
Complete the table below.

Total Federal Financial Support	**$**

Question 10: Explanation of Calculation of Federal Financial Support

Disaggregate the total Federal financial support amount reported above by the amounts allocated to the sources in the list below. Please list amounts in order of magnitude. In addition, describe assumptions, methodological steps, and other information needed to calculate the estimates provided in Question 9. If you report a value in "Other Federal Financial Support Not Otherwise Included Elsewhere" in your response to this question, please list the source(s) of that Federal financial support. Please include the identification number for grants and comparable awards.

- Tax credits (General, R&D)
- Orphan Drug Act and Other Specific Tax Credits
- National Institutes of Health (NIH) Funding
- Department of Defense (DOD) Congressionally Directed Medical Research (CDMR) Funding
- Biomedical Advanced Research and Development Authority (BARDA) Funding
- Defense Advanced Research Projects Agency (DARPA) Funding
- Other Federal Financial Support Not Included Elsewhere
- Federal Financial Support for failed products related to the selected drug

Federal Financial Support	**RESPONSE FORMAT** *Text (5,000-word limit)*

Question 11: Agreements Between Primary Manufacturer and Federal Government
List and describe each licensing agreement, pricing agreement, purchasing agreement, and other agreement in place between your company and any federal government agency related to the discovery, research, and/or development of the selected drug. Add additional rows to your response to Question 11 as needed.

- In the "Nature of Agreement" field, please provide details on the terms of the agreement, such as information on pricing, the nature and amount of goods/services agreed upon, timelines to delivering goods/services, conditions on the agreement (exclusivity, sole supplier, etc.) and effective dates and expiration dates, if applicable. For example, this field could detail an agreement between the Primary Manufacturer and Federal Government where the Primary Manufacturer agrees to produce a certain quantity of a drug that is being developed and has not yet been approved or licensed, deliver it to the Federal Government within a specified timeline, and not contract with other state or local governmental entities or insurers while this agreement is in place.

Type of Agreement	**Federal Agency(ies) Participating in Agreement**	**Nature of Agreement**
Drop down menu of agreement options: licensing, pricing, purchasing, other	*Text (100-word limit)*	*Text (1,000-word limit)*

F. Patents, Exclusivities, and Approvals

Primary Manufacturer Response Required

Section F focuses on capturing data on the selected drug related to pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals under section 505(c) of the Federal Food, Drug, and Cosmetic (FD&C) Act or section 351(a) of the Public Health Service (PHS) Act. Follow the instructions below when answering Questions 12 through 15.

Definitions for Section F:

- CMS considers relevant patents, both expired and unexpired, and relevant patent applications to include:
  - All patents issued by the United States Patent and Trademark Office (USPTO), as of September 1, 2023, both expired and unexpired, for which a claim of patent infringement could reasonably be, or has been, asserted against a person or manufacturer engaged in the unlicensed manufacture, use, or sale of the selected drug in any form or any person or manufacturer seeking FDA approval of a product that references the selected drug.
  - All patents related to the selected drug, both expired and unexpired, where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product or if any patents related to the selected drug are held by a federal agency).
  - All patent applications related to the selected drug that are pending issuance by the USPTO.
  - Patents and patent applications related to the selected drug include, but are not limited to, any patents that are, have been, or may be listed for the selected drug in

the FDA Orange Book or Purple Book;[16] utility patents that claim the drug product (formulation or composition), drug substance (active ingredient), metabolites or intermediaries of a selected drug, method(s) of using the drug, or method(s) of manufacturing the drug; and design patents that, for example, claim a design on the packaging of the selected drug

- Exclusivity periods under the FD&C Act or the PHS Act refer to certain delays and prohibitions on the approval of competitor drug products. An NDA or BLA holder is eligible for exclusivity if statutory requirements are met. Exclusivities include:
  - Orphan Drug Exclusivity (ODE);[17]
  - New Chemical Entity Exclusivity (NCE);[18]
  - Generating Antibiotic Incentives Now (GAIN) Exclusivity for Qualified Infectious Disease Products (QIDP);[19]
  - New Clinical Investigation Exclusivity (NCI);[20]
  - Pediatric Exclusivity (PED);[21] and
  - Reference Product Exclusivity for Biological Products.[22]
- Active and pending FDA applications and approvals includes:
  - all applications for approval under section 505(c) of the FD&C Act or sections 351(a) of the PHS Act, including those not yet decided.

Instructions for Section F:

- For Questions 12 through 15, the relevant time period for reporting begins on the later of the date that basic pre-clinical research began on the selected drug or the date the selected drug was acquired by the Primary Manufacturer and ends on the date the most recent NDA / BLA was approved for the selected drug.
- For Questions 12 through 15, include required data for the selected drug.

Question 12: Patents (Expired and Non-Expired) and Patent Applications

In the table below, please list each patent that is related to the selected drug, as well as each application for a patent related to the selected drug that is pending with the USPTO. Patents and patent applications related to the selected drug that should be listed below include, but are not limited to, utility patents that claim the drug product (formulation or composition), drug substance (active ingredient), metabolites or intermediaries of a selected drug, method(s) of using the drug, or method(s) of manufacturing the drug, as well as any design patents that, for example, claim a design on the packaging of the selected drug. Any patents or patent applications related to the selected drug where the Primary Manufacturer is not listed as the assignee/applicant (for example, for a joint venture product or if any patents related to the

[16] FDA serves a ministerial role with regard to the listing of patent information in the Orange Book and Purple Book.
[17] Section 527 of the FD&C Act.
[18] Section 505(c)(3)(E)(ii) and Section 505(j)(5)(F)(ii) of the FD&C Act.
[19] Section 505E(a) of the FD&C Act.
[20] Section 505(c)(3)(E)(iii) & (iv) and Section 505(j)(5)(F)(iii) & (iv) of the FD&C Act.
[21] Section 505A(b) & (c) of the FD&C Act.
[22] Section 351(k)(7) of the PHS Act.

selected drug are held by a federal agency) must be listed below. Any patents that are or have been listed for the selected drug in the FDA Orange Book or Purple Book must be included in the table below. For each entry, indicate whether the patent claims the drug product, drug substance, and/or a method of use of the selected drug. For each patent (expired or unexpired) and pending patent application listed in the table below, please upload a PDF file of the USPTO patent application. Do not include patent applications which were denied. Add additional rows to your response to Question 12 as needed.

Patent Number	**Date Filed**	**Patent Expiry Date**	**Drug Product Patent**	**Drug Substance Patent**	**Drug Method of Use Patent**	**Patent Application Pending**	**Patent Type**	**Listed in FDA Orange Book/Purple Book**	**Patent Application**
#	MM/DD/YYYY	MM/DD/YYYY	Yes/No Flag	Yes/No Flag	Yes/No Flag	Yes/No Flag	Drop down menu of patent types. Options: Utility, Design	Yes/No Flag	Upload corresponding patent application.

Question 13: Explanation of Patents (Expired and Non-Expired) and Patent Applications
If applicable, please provide additional information about the patent applications reported in the table above and describe how they relate to the selected drug. This information can include further information on the purpose of the patent, for example, if the patent claims a specific indication(s) of the selected drug or a device used to administer the selected drug, or other information that will be helpful to understand how the patent contributes to the selected drug. As applicable, please also use this free response field to indicate which patents related to the selected drug are held by a federal agency and describe how they relate to the selected drug.

FIELD	**RESPONSE FORMAT**
Explanation of patents	*Text (1,000-word limit)*

Question 14: Regulatory Exclusivity Periods
As applicable, please report all regulatory exclusivity periods under the FD&C Act or the PHS Act that are listed in the Orange Book or the Purple Book and in effect or have expired for the selected drug.[23] *Complete table for Question 14 by adding rows as needed.*

[23] With respect to biological products, CMS understands that FDA has not made a determination of first licensure for each 351(a) biological product included in the Purple Book. The absence of a date of first licensure in the Purple Book does not mean that a biological product on the list is not, or was not, eligible for reference product exclusivity.

Type of Exclusivity	Exclusivity Expiration Date	Application (NDA / BLA) Number	NDC-9s Covered by Exclusivity	Comments
Drop down menu of exclusivity types. Options: Orphan Drug Exclusivity, New Chemical Entity Exclusivity, GAIN Exclusivity for Qualified Infectious Disease Products, New Clinical Investigation Exclusivity, Pediatric Exclusivity, Reference Product Exclusivity for Biological Products	*MM/DD/YYYY*	*#*	*Text*	*Text (300-word limit)*

Question 15: All Active and Pending FDA Applications and Approvals
List all active and pending FDA applications and approvals for the selected drug under section 505(c) of the FD&C Act and 351(a) of the PHS Act.

- Include all applications for approval under section 505(c) of the FD&C Act or section 351(a) of the PHS Act, including those not yet decided. Leave approval date blank for those applications not yet decided. *[Complete table for Question 15 by adding rows as needed using the indicated format]*
- Please submit any efficacy supplements that have been approved or are pending FDA approval but exclude manufacturing supplements.

Application (NDA / BLA) Number	**Application Type (NDA; BLA)**	**Classification Code[24]**	**Approval Date**	**Indication**	**Dosage Form and Strength**	**Sponsor**	**Application Status**	**Comments**
#	*Drop down menu of application types. Options: NDA, BLA*	Select one or more of the following options: Options: Type 1 — New Molecular Entity, Type 2 — New Active Ingredient, Type 3 — New Dosage Form, Type 4 — New Combination, Type 5 — New Formulation or Other Differences (e.g., new indication, new applicant, new manufacturer), Type 6 — New Indication or Claim, Same Applicant, Type 7 — Previously Marketed But Without an Approved	*MM DD, YYYY*	*Text*	*Text*	*Text*	*Select one of the following options: approved, tentatively approved, pending, withdrawn, or other*	*Text (300-word limit)*

[24] These classification code options will only be available if the "NDA" application type is selected. If "BLA" is selected, this dropdown will be grayed out as BLAs do not use classification codes.

Application (NDA / BLA) Number	Application Type (NDA; BLA)	Classification Code[24]	Approval Date	Indication	Dosage Form and Strength	Sponsor	Application Status	Comments
		NDA, Type 8 — Rx to OTC, Type 9 — New Indication or Claim, Drug Not to be Marketed Under Type 9 NDA After Approval, Type 10 — New Indication or Claim, Drug to be Marketed Under Type 10 NDA After Approval						

G. Market Data and Revenue and Sales Volume Data

Primary Manufacturer Response Required

The purpose of Questions 16 through 25 in this section is to collect the market data and revenue and sales volume data described in section 1194(e)(1)(E) of the Act.

Definitions for Section G:

- Wholesale Acquisition Cost (WAC) unit price: The manufacturer's list price for the drug or biological product to wholesalers or direct purchasers in the United States, not including prompt pay or other discounts, rebates or reductions in price, for the most recent month for which the information is available, as reported in wholesale price guides or other publications of drug or biological product pricing data (as defined in section 1847A(c)(6)(B) of the Act). The WAC unit price is reported at the NDC-11 level.

- National Council of Prescription Drug Programs Billing Unit Standards (NCPDP): The three NCPDP Billing Unit Standards (BUS)[25] are: each (EA), milliliter (ML), and gram (GM). For certain volume data of the selected drug, CMS is requesting units be reported using the NCPDP BUS to facilitate comparison with the amounts in the quantity dispensed field found in PDE data, which also uses the NCPDP BUS.
- Medicaid best price: The Medicaid best price is defined in 42 C.F.R. § 447.505(a). The Medicaid best price is reported at the NDC-9 level.
- Average manufacturer price (AMP) unit: The unit type used by the manufacturer to calculate AMP (42 C.F.R. § 447.504) and best price (42 C.F.R. § 447.505) for purposes of the Medicaid Drug Rebate Program (MDRP): injectable anti-hemophilic factor, capsule, suppository, gram, milliliter, tablet, transdermal patch, each, millicurie, microcurie. Such units are reported by the manufacturer on a monthly basis at the NDC-9 level.
- Federal supply schedule (FSS) price: The price offered by the VA in its FSS program, by delegated authority of the General Services Administration.[26] The FSS price is reported at the NDC-11 level.
- Big Four price"): The Big Four price is described in 38 U.S.C. § 8126. The Big Four Price is reported at the NDC-11 level.[27]
- U.S. commercial average net unit price: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the average net unit price of the selected drug for group or individual commercial plans on- and off-Exchange, excluding Medicare fee-for-service (Parts A and B), Medicare Advantage, Medicare Part D, Medicaid fee-for-service, and Medicaid managed care. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any purchasers. The U.S. commercial average net unit price is reported at the NDC-11 level.
- U.S. commercial average net unit price— without patient assistance program: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the U.S. commercial average net unit price net of manufacturer-run patient assistance programs that provide financial assistance such as coupons and co-payment assistance or free drug products to patients offered by the Primary Manufacturer and any Secondary Manufacturer(s). The U.S. commercial average net unit price— without patient assistance program is reported at the NDC-11 level.
- U.S. commercial average net unit price— best: For the sole purpose of data collection under section 1194(e)(1)(E) of the Act, the lowest U.S. commercial average net unit price

[25] See: https://standards.ncpdp.org/Billing-Unit-Request.aspx#:~:text=Billing%20Unit%20Requests,grams%22%20or%20%22milliliters.%22.
[26] See: https://www.fss.va.gov/index.asp.
[27] The Big Four price is the maximum price a drug manufacturer is allowed to charge the Big Four federal agencies, which are the Department of Veterans Affairs, the Department of Defense, the Public Health Services, and the Coast Guard. See: https://www.cbo.gov/publication/57007.

offered by the Primary Manufacturer and any Secondary Manufacturer(s) to any commercial payer in the U.S. The average net unit price must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by the Primary Manufacturer or any Secondary Manufacturer(s) to any purchasers. The U.S. commercial average net unit price─ best is reported at the NDC-11 level.

Instructions for Section G:

- For the purpose of answering Questions 16 through 25, please also follow the instructions specific to each question.
- Use the list of definitions in the "Definitions for Section G. Market Data and Revenue and Volume Data" section to answer the questions.
- For Question 16 through 25, information for the Primary Manufacturer and any Secondary Manufacturer(s) must be reported.
- For Questions 17, 19, 21, 23, and 25, please include not applicable (N/A) in the free response field if no explanation is necessary.

Question 16: Wholesale Acquisition Cost Unit Price
Follow the instructions below when providing responses in the following table about the WAC unit price of the selected drug:

- Any deviation from the reported WAC unit price in the table below and the WAC unit price as reported in wholesale price guides or other publications of drug or biological price data must be explained in Question 17 so that CMS can understand the reasons for these differences.
- Units must be reported in one of the three NCPDP BUS: each (EA), milliliter (ML), or gram (GM). The unit type reported must be specified for each of the NDC-11s associated with the selected drug. Total unit volume must be the total number of units sold to wholesalers and direct purchasers during the quarter. Please do not include units associated with free samples in the calculated prices or reported total unit volume.
- Include a row for each NDC-11 and each quarter during the most recent five years if the NDC-11 was marketed, sold, or distributed at any time during the most recent five years and complete all fields. If the NDC-11 was not marketed, sold, or distributed to any wholesaler or direct purchaser in a particular quarter, please still include a row for this particular quarter, and enter the NDC-11, quarter, and unit type information, but enter "0" in the total unit volume field and leave the WAC field blank.

NDC-11	**Quarter**	**WAC**	**Unit type (each, ML, GM)**	**Total Unit Volume**
12345-6789-01	*QQ/YYYY*	*$*	*Drop down (each, ML, GM)*	*#*

Question 17: Explanation of Information Reported in Question 16: Wholesale Acquisition Cost Unit Price

If applicable, describe assumptions, methodological steps, and other information necessary to explain the deviation between the WAC unit price provided in response to Question 16 and those found in available drug databases (e.g., Medi-Span, First Databank, RED BOOK).

FIELD	RESPONSE FORMAT
Explanation of WAC unit price data	*Text (1,000-word limit)*

Question 18: Medicaid Best Price

Was a Medicaid best price determination ever made for a calendar quarter for the selected drug during the most recent five years?

RESPONSE FORMAT
Yes/No

(If response is Yes, please fill out the following tables. If response is No, please skip to Question 20) Follow the instructions below when providing responses in the following table about the Medicaid best price of the selected drug:

- The Medicaid best price information must reflect what was submitted to Medicaid under the MDRP in accordance with the Medicaid National Drug Rebate Agreement and as described in section 42 C.F.R. § 447.505 – Determination of best price. The reported Medicaid best price in the table below must reflect any restatements that have been certified under the MDRP.
- Please report Medicaid best price information using the same unit type used to report AMP and Medicaid (i.e., injectable anti-hemophilic factor, capsule, suppository, gram, milliliter, tablet, transdermal patch, each, millicurie, microcurie). Total unit volume for the quarter is the sum of monthly AMP units reported to the MDRP for the quarter.
- Include a row for each NDC-9 and each quarter during the most recent five years if a Medicaid best price determination was made at any time during the most recent five years for that NDC-9 and complete all fields. If the NDC-9 did not have a Medicaid best price determination in a particular quarter, please still include a row for this particular quarter and enter NDC-9, quarter, and unit type information, but enter "0" in the total unit volume field and leave the Medicaid best price field blank.

NDC-9	Quarter	Medicaid Best Price	Unit Type	Total Unit Volume
12345-6789	*QQYYYY*	*$*	*Text*	*#*

Question 19: Explanation of Information Reported in Question 18: Medicaid Best Price
If applicable, describe other information you feel is necessary to interpret reported information in response to Question 18.

FIELD	RESPONSE FORMAT
Explanation of Medicaid Best Price data	*Text (1,000-word limit)*

Question 20: Federal Supply Schedule Price
Was a Federal supply schedule (FSS) price for the selected drug ever available during the most recent five years?

RESPONSE FORMAT
Yes/No

(If response is Yes, please fill out the following tables. If response is No, please skip to Question 22) Follow the instructions below when providing responses in the following table about FSS prices of the selected drug:

- The FSS price information must reflect what can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.[28]
- Units must be reported in one of the three NCPDP BUS: each (EA), milliliter (ML), or gram (GM). The unit type reported must be specified for each of the NDC-11s associated with the selected drug. Total unit volume is the total number of units (i.e., EA, ML, or GM) for each NDC-11 sold to direct federal purchasers. Please do not include units associated with free samples in the reported total unit volume.
- Include a row for each NDC-11 and price period that occurred during the most recent five years.

NDC-11	Price Start Date to End Date	Federal Supply Schedule Service Price	Unit Type (EA, ML, GM)	Total Unit Volume
12345-6789-01	*MMDDYYYY-MMDDYYYY*	*$*	*Drop down (EA, ML, GM)*	*#*

Question 21: Explanation of Information Reported in Question 20: Federal Supply Schedule Price
If applicable, describe other information you feel is necessary to interpret reported information in response to Question 20.

FIELD	RESPONSE FORMAT
Explanation of federal supply schedule price data	*Text (1,000-word limit)*

[28] See: https://www.va.gov/opal/nac/fss/pharmprices.asp.

Question 22: Big Four Price
Was a Big Four price ever available for the selected drug during the most recent five years?

RESPONSE FORMAT
Yes/No

(If response is Yes, please fill out the following tables. If response is No, please skip to Question 24) Follow the instructions below when providing responses in the following table about the Big Four price of the selected drug:

- The Big Four price information must reflect the information that can be found online in the pharmaceutical pricing data for all VA National Acquisition Center programs.[29]
- Units must be reported in one of the three NCPDP BUS: each (EA), milliliter (ML), or gram (GM). The unit type reported must be specified for each of the NDC-11s associated with the selected drug. Total unit volume is the total number of units (i.e., EA, ML, or GM) for each NDC-11 sold to the Big Four federal agencies (Department of Veterans Affairs, Department of Defense, the Public Health Service, and the Coast Guard). Please do not include units associated with free samples in the reported total unit volume.
- Include a row for each NDC-11 and price period that occurred during the most recent five years.

NDC-11	Price Start Date to Price End Date	Big Four Price	Unit Type EA, ML, GM)	Total Unit Volume
12345-6789-01	*MMDDYYYY-MMDDYYYY*	*$*	*Drop down (EA, ML, GM)*	*#*

Question 23: Explanation of Information Reported in Question 22: Big Four Price
If applicable, describe other information you feel is necessary to interpret reported information in response to Question 22.

FIELD	RESPONSE FORMAT
Explanation of Big Four price data	*Text (1,000-word limit)*

Question 24: U.S. Commercial Average Net Unit Price
Follow the instructions below when providing responses in the following table about the U.S. commercial average net unit price, including group and individual commercial plans on- and off-Exchange of the selected drug:

[29] See: https://www.va.gov/opal/nac/fss/pharmprices.asp.

- Exclude price and volume information for the selected drug for Medicare fee-for-service (Parts A and B), Medicare Advantage, Medicare Part D, Medicaid fee-for-service, and Medicaid managed care.
- Include a row for each NDC-11 and each quarter during the most recent five years if the NDC-11 was ever marketed, sold, or distributed at any time during the most recent five years and complete all fields. If the NDC-11 was not marketed, sold, or distributed in a particular quarter, please still add include a row for this particular quarter, and enter the NDC-11, quarter, and unit type information, but enter "0" in the total unit volume field and leave the three price fields blank.
- Units must be reported in one of the three NCPDP BUS: each (EA), milliliter (ML), or gram (GM). The unit type reported must be specified for each of the NDC-11s associated with the selected drug. Please do not include units associated with free samples in the calculated prices or reported total unit volume.
- The NDC-11 price reported in the U.S. commercial average net unit price field must be net of discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered by Primary Manufacturer or any Secondary Manufacturer(s) to any purchasers.
- If the Primary Manufacturer or Secondary Manufacturer(s) provided manufacturer-run financial assistance such as coupons and co-payment assistance or free drug products to patients, separately report the price net of coupons and co-payment assistance to patients in the U.S. commercial average net unit price─ without patient assistance programs field. If the Primary Manufacturer and Secondary Manufacturer(s) did not provide coupons or co-payments assistance to patients, please leave the U.S. commercial average net unit price─ without patient assistance programs field blank.
- Provide the lowest price that the Primary Manufacturer or any Secondary Manufacturer(s) made available to any commercial payer during the quarter in the U.S. commercial average net unit price─ best field.

NDC-11	**Quarter**	**U.S. Commercial Average Unit Net Price**	**U.S. Commercial Average Net Unit Price- Without Patient Assistance Programs**	**U.S. Commercial Average Net Unit Price- Best**	**Unit type (EA, ML, GM)**	**Total Unit Volume**
12345-6789-01	*QQYYYY*	*$*	*$*	*$*	*Drop down (EA, ML, GM)*	*#*

Question 25: Explanation of Information Reported in Response to Question 24: U.S. Commercial Average Net Unit Price

Describe assumptions, methodological steps, and other information for the following topics related to Question 24:

- How sales to enrollees of group and individual commercial plans on- and off-Exchange were determined.
- How discounts, chargebacks or rebates, cash discounts, free goods contingent on a purchase agreement, up-front payments, coupons, goods in kind, free or reduced-price services, grants, or other price concessions or similar benefits offered to any purchasers were allocated across NDC-11s and quarters.
- If applicable, how coupons and co-payment assistance to patients were allocated across NDC-11s and quarters.
- How all of this information was used to calculate the U.S. commercial average net unit price and U.S. commercial average net unit price─ without patient assistance programs and determine the U.S. commercial average net unit price─ best.

FIELD	RESPONSE FORMAT
Explanation of U.S. commercial average net unit price data	*Text (1,000-word limit)*

H. Certification of Submission of Sections A through G for Primary Manufacturers

Required for Primary Manufacturers

Instruction for Section H:
An individual eligible to certify this submission on behalf of the Primary Manufacturer must be one of the following: (1) the chief executive officer (CEO) of the Primary Manufacturer, (2) the chief financial officer (CFO) of the Primary Manufacturer, (3) an individual other than a CEO or CFO, who has authority equivalent to a CEO or a CFO, or (4) an individual with the directly delegated authority to perform the certification on behalf of one of the individuals mentioned in (1) through (3).

Certification:
I hereby certify, to the best of my knowledge, that the information being sent to CMS in this submission is complete and accurate, and the submission was prepared in good faith and after reasonable efforts. 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 payment purposes, including determination of a maximum fair price, as defined in section 1191(c)(3) of the Social Security Act. I also certify that I will timely notify CMS if I become aware that any of the information submitted in this form has changed. I also understand that any misrepresentations may also give rise to liability, including under the False Claims Act.

Yes [ ]
No [ ]

Contact Information to be entered:

Field	Response
Name of the Person Responsible for the Submission	*Text*
Title	*Text*
Telephone	*Text*
Email	*Text*
Signature	*Text*
Date	*MMDDYYYY*

I. Evidence About Alternative Treatments

Optional for All Respondents, Including Primary Manufacturer

While CMS is seeking public input under section 1194(e)(2) of the Act to consider information on the selected drug and its pharmaceutical therapeutic alternative(s), please limit your response and do not include personally identifiable information[30] (PII) or protected health information[31] (PHI). CMS will collect only the minimum necessary information related to the selected drug and its therapeutic alternative(s) for the purpose of implementing and operating the Negotiation Program and will not retrieve evidence for manufacturer negotiations by personal identifier (PII or PHI). CMS will not, through this collection, create or maintain a system of records as understood by the Privacy Act of 1974 and accompanying Office of Management and Budget guidance.

Each interested party will be able to answer each of the questions in Section I one-time for each selected drug.

Question 26: Respondent Information
Required: Individuals or organizations, including manufacturers, that wish to provide information in this Section I must provide the following information.[32]

FIELD	RESPONSE FORMAT
Selected Drug	*TEXT*
Respondent Name	*TEXT*
Organization Name (if applicable)	*TEXT*
Respondent Email	*TEXT*

[30] Personally identifiable information (PII) is information, including demographic data, that relates to the individual's past, present, or future physical or mental health or condition; the provisions of health care to the individual; or the past, present, or future payment for the provision of health care to the individual, and that identifies the individual or for which there is a reasonable basis to believe it can be used to identify the individual. PII includes many common identifiers such as name, address, birth date, Social Security Number, etc. See https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html.
[31] Protected health information is individually identifiable health information held or transmitted by a covered entity or its business associate, in any form or media, whether electronic, paper, or oral. See https://www.hhs.gov/hipaa/for-professionals/privacy/laws-regulations/index.html.
[32] This section will be included in the Primary Manufacturer's CMS HPMS negotiation module, and the Primary Manufacturer must submit any responses to the questions in this section there.

Optional: Check the relevant box: Which of the following best describes the person completing this form?

[ ] Representative of a manufacturer that does not manufacture the selected drug or its therapeutic alternative(s)

[ ] Representative of a manufacturer of the selected drug or its therapeutic alternative(s)

[ ] Representative of a trade association

[ ] Representative of a patient advocacy organization

[ ] A health care provider who has experience prescribing, dispensing, or administering the selected drug or its therapeutic alternative(s)

[ ] A patient who has experience taking the selected drug or its therapeutic alternative(s)

[ ] A caregiver for an individual who has experience taking the selected drug or its therapeutic alternative(s)

[ ] Academic researcher or other subject matter expert not affiliated with a manufacturer of the selected drug or its therapeutic alternative(s)

[ ] Academic researcher or other subject matter expert affiliated with a manufacturer of the selected drug or its therapeutic alternative(s)[33]

[ ] Other

Instructions for Questions 27 through 31:

Please follow the instructions below when answering these questions.

- The following questions are optional. You may answer some or all of the questions. Enter "No response" if you do not wish to respond to a given question.
- Please answer each question in narrative (text) form. Your responses will be limited to the word and citation maximums provided for each question.
- Submissions for Section I may include, but are not limited to, published or unpublished material such as peer-reviewed articles, whitepapers, case studies, and government reports. Please note that CMS reserves the right to review submitted materials for relevance and in accordance with the standards outlined in section 50.2 of the revised guidance.
- Please provide citations to published material rather than copies of articles. The respondent is responsible for ensuring that their submission complies with applicable law, including, but not limited to, copyright law. If data are unpublished, clearly indicate this in the citation. For unpublished data without a citation, please summarize key findings as

[33] For the purpose of this ICR "affiliated with the manufacturer" means an individual who receives or has received funding from the manufacturer for research, speaking, or other engagements, and/or any other purpose related to the selected drug or its potential therapeutic alternative(s); or any individual who has been asked to respond to this ICR or otherwise advise the manufacturer of a selected drug on the Negotiation Program, regardless of compensation.

appropriate in your response to Questions 28 through 30 and upload any relevant visual representations as additional materials as described below.

- Respondents are requested to provide citations in response to Questions 28 through 30 in the MLA style format appropriate for the source of information (e.g., a journal article). Information on how to format citations is available for free through the National Library of Medicine at: https://www.ncbi.nlm.nih.gov/books/NBK7256/.
- When information in the free text response for Questions 28 through 30 is supported by a citation reported in response to that question, please label the end of the sentence in the free text response with a number (e.g., [1], [2]) that corresponds to the number assigned to the citations provided for that same question.
- CMS will review submitted studies that use cost-effectiveness measures to determine if the study is relevant to the selected drug and/or its therapeutic alternative(s) and to ensure the cost-effectiveness measure used does not value extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than an individual who is younger, nondisabled, or not terminally ill. Respondents must indicate if their submission includes any cost-effectiveness measures. Respondents are also requested to provide a short description of any cost-effectiveness measures included in the research submitted and the utility they believe the data provides in reviewing the selected drug without treating extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill. Cost-effectiveness measures include but are not limited to quality-adjusted life-years (QALYs), Equal Value of Life-Years Gained (evLYG), Equal Value Life-Year (evLY), and Health Years in Total (HYT).
- CMS will not use 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.[34] Information submitted that treats extending the life of individuals in these populations as of lower value, for example, QALYs will not be used. In instances where a study includes a measure such as QALYs but has clearly separated QALYs or other measures that treat extending the life of individuals who are elderly, disabled, or terminally ill as of lower value from other evidence in the report (e.g., clinical effectiveness, risks, harms, etc.) that is relevant to the factors listed in section 1194(e)(2) of the Act, CMS will consider such separate evidence. In these cases, indicate clearly in the in-text citation if the evidence provided 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 and clearly indicate what separate evidence CMS might consider.
- All declarative statements must be supported by evidence with a citation, unless you are sharing a personal experience with prescribing or taking the selected drug and/or its therapeutic alternative(s) or you are a caregiver describing the experience of the person taking the selected drug and/or its therapeutic alternative(s).

[34] Section 1194(e)(2) of the Social Security Act.

- Submissions may include visual representations of the information, including tables, charts, and/or graphs in Questions 28 through 30. The information submitted in the space for visual representations should only include the table/chart/graph, and no additional text. CMS will not review any additional text included. PDF files will be accepted within specified file size limits for visual representations. The main text response for Questions 28 through 30 should include clear numbers/references to the tables/charts/graphs submitted.
- When citing studies to support responses, briefly summarize the study context and relevant comparator or therapeutic alternative drug(s) studied, as applicable.
- Indicate in your response if a portion of a response applies to specific dosages, forms, strengths, and/or indications of a selected drug or its therapeutic alternative(s).

Question 27: Prescribing Information

Definitions:

- Therapeutic Alternative: A therapeutic alternative must be a pharmaceutical product that is clinically comparable to the selected drug. CMS will consider different therapeutic alternatives for each indication, as applicable. Therapeutic alternatives may be a brand name drug or biological product, generic drug, or biosimilar and may be on-label or off-label to treat a given indication. CMS will begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes. In cases where there are many potential therapeutic alternatives for a given indication of the selected drug, CMS may focus on a subset of therapeutic alternatives that are most clinically comparable to the selected drug.

Additional information regarding identification of indications for a selected drug and its pharmaceutical therapeutic alternative(s) is described in section 60.3.1 of the revised guidance.

Instructions for Question 27:

- Specify whether you are referencing the selected drug or a pharmaceutical therapeutic alternative(s) for each indication(s) you are referencing when discussing FDA prescribing information.

Questions on Prescribing Information:

- What prescribing information has been approved by the FDA for the selected drug and for therapeutic alternative(s) to the selected drug?
- Please provide information about how the selected drug and its therapeutic alternative(s) are used in the course of care for the condition or disease treated by each indication.

- If the selected drug is used off-label to treat a certain disease or condition, please indicate this and provide evidence from nationally recognized, evidence-based guidelines and recognized by CMS-approved Part D compendia, as applicable.[35]

FIELD	RESPONSE FORMAT
Response to Question 27	*Text* (3,000-word limit)

Does the evidence submitted include a cost-effectiveness measure:
[ ] Yes
[ ] No
[ ] Don't know

If yes to the question above, please select the applicable statement.
[ ] The evidence submitted includes QALYs or other cost-effectiveness measures that treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

[ ] The evidence submitted includes cost-effectiveness measures that DO NOT treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

Question 28: Therapeutic Impact and Comparative Effectiveness

Definitions:

- Therapeutic Alternative: A therapeutic alternative must be a pharmaceutical product that is clinically comparable to the selected drug. CMS will consider different therapeutic alternatives for each indication, as applicable. Therapeutic alternatives may be a brand name drug or biological product, generic drug, or biosimilar and may be on-label or off-label to treat a given indication. CMS will begin by identifying therapeutic alternatives within the same drug class as the selected drug based on properties such as chemical class, therapeutic class, or mechanism of action before considering therapeutic alternatives in other drug classes. In cases where there are many potential therapeutic alternatives for a given indication of the selected drug, CMS may focus on a subset of therapeutic alternatives that are most clinically comparable to the selected drug.
- Outcomes: Outcomes may be clinical or related to the functioning, symptoms, quality of life, or other aspects of a patient's life. Outcomes such as cure, survival, progression-free survival, or improved morbidity could be considered when comparing the selected drug to its therapeutic alternative(s). Outcomes such as changes in symptoms or other factors that are of importance to patients, and patient-reported outcomes will also be identified and considered in determining clinical benefit, if available. Additional outcomes such as

[35] CMS-approved Part D compendia are listed in Chapter 6 of the Prescription Drug Benefit Manual as described in 1927(g)(1)(B)(i) of the Act.

changes to productivity, independence, and quality of life will also be considered, including patient-centered outcomes when available, to the extent that these outcomes correspond with a direct impact on individuals taking the drug. The caregiver perspective will be considered when there is a direct impact on the individuals taking the selected drug or therapeutic alternatives.

- Patient-centered outcome: An outcome that is important to patients' survival, functioning, or feelings as identified or affirmed by patients themselves, or judged to be in patients' best interest by providers and/or caregivers when patients cannot report for themselves.[36]

Additional information regarding identification of indications for a selected drug and its pharmaceutical therapeutic alternative(s) is described in section 60.3.1 of the revised guidance.

Instructions for Question 28:

- Specify the therapeutic alternative and indication of the selected drug that you are discussing.
- When discussing the therapeutic impact of the selected drug, indicate outcome(s) used, the indication(s) to which the evidence applies, and the therapeutic alternative(s) to which the evidence applies.

Questions on Therapeutic Impact and Comparative Effectiveness:

- Please provide information on the therapeutic impact of the selected drug compared to existing therapeutic alternatives. What is known about the comparative effectiveness of the selected drug and its therapeutic alternative(s)? Please discuss for each indication of the selected drug, as applicable. Consider discussing outcomes (including patient-reported outcomes) and patient experience for each indication, as applicable.
- Please provide key outcomes for each indication of the selected drug, as applicable, and explain why each outcome was chosen.
- To what extent does the selected drug represent a therapeutic advance as compared to existing therapeutic alternatives? Please discuss for each indication of the selected drug, as applicable.
- Please provide information on the risks, harms, or side effects, and any unique scenarios or considerations related to clinical benefit, safety, and patient experience related to the selected drug and its therapeutic alternative(s) for each indication, as applicable. Please describe any differences in the safety profile of the selected drug and its therapeutic alternative(s) for each indication, as applicable.
- Please provide current costs of such existing therapeutic alternatives (if known).

FIELD	**RESPONSE FORMAT**
Response to Question 28	*Text* (3,000-word limit)
Additional Materials for Question 28	*Text* (Up to 50 citations; up to 10 tables/charts/graphs)

[36] ISPOR Plenary, Patrick (2013) via FDA's "Patient-Focused Drug Development: Collecting Comprehensive and Representative Input – Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders," June 2020. See: https://www.fda.gov/media/139088/download.

Does the evidence submitted include a cost-effectiveness measure:
[ ] Yes
[ ] No
[ ] Don't know

If yes to the question above, please select the applicable statement.
[ ] The evidence submitted includes QALYs or other cost-effectiveness measures that treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

[ ] The evidence submitted includes cost-effectiveness measures that DO NOT treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

Question 29: Comparative Effectiveness on Specific Populations

Definitions:

- Specific populations: Specific populations include individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations among Medicare beneficiaries including those that may experience disparities in access to care, health outcomes, or other factors when taking the selected drug that impact health equity.
- Health equity: The attainment of the highest level of health for all people, where everyone has a fair and just opportunity to attain their optimal health regardless of race, ethnicity, disability, sexual orientation, gender identity, socioeconomic status, geography, preferred language, or other factors that affect access to care and health outcomes.[37]

Instructions for Question 29:

- Specify which specific population and which indication of the selected drug you are discussing.

Questions on Comparative Effectiveness on Specific Populations:

- What is known about the comparative effectiveness of the selected drug and therapeutic alternatives to the selected drug with respect to specific populations, such as individuals with disabilities, the elderly, individuals who are terminally ill, and children?
- Are there other specific populations not noted in the question above that use the selected drug that could be considered? If so, please explain.
- As applicable, for other specific populations that use the selected drug, what is known about comparative effectiveness of the selected drug and its therapeutic alternative(s)?
- What health equity considerations should CMS consider related to specific populations taking the selected drugs? This may include, but is not limited to, challenges or

[37] See: https://www.cms.gov/pillar/health-equity.

advantages accessing the drug compared to therapeutic alternatives, differences in clinical or other outcomes, or differences in disease or condition symptoms for a specific population that the drug does or does not adequately address.
- In addition to comparative effectiveness, please discuss any differences in the safety profile of the selected drug compared to its therapeutic alternative(s) for each applicable specific population.

Field	Response
Response to Question 29	*Text* (3,000-word limit)
Additional Materials for Question 29	*Text* (Up to 50 citations; up to 10 tables/charts/graphs)

Does the evidence submitted include a cost-effectiveness measure:
[ ] Yes
[ ] No
[ ] Don't know

If yes to the question above, please select the applicable statement.
[ ] The evidence submitted includes QALYs or other cost-effectiveness measures that treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

[ ] The evidence submitted includes cost-effectiveness measures that DO NOT treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

Question 30: Addressing Unmet Medical Needs

Definitions for Question 30:

- Unmet medical need: A drug or biological product may be considered to meet an unmet medical need if the drug or biological product treats a disease or condition in cases where no other treatment options exist or existing treatments do not adequately address the disease or condition.[38] Unmet medical need is determined at the time of submission of this information.

Instructions for Question 30:

- Specify the therapeutic alternative and indication of the selected drug that you are discussing, if applicable.

[38] CMS will consider the nonbinding recommendations in the FDA "Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics" (May 2014) when considering if a drug addresses an unmet medical need for the purpose of the Negotiation Program.

- When discussing the therapeutic impact of the selected drug, indicate outcome(s) used, the indication(s) to which the evidence applies, and the therapeutic alternative(s) to which the evidence applies.

Questions on Addressing Unmet Medical Needs:

- Does the selected drug address an unmet medical need for any indications; and if so, which indications?
- To what extent do the selected drug and therapeutic alternative(s) to the selected drug address an unmet medical need for an indication, as applicable?
- If unmet medical need is determined based on inadequate therapeutic alternative(s), please explain why therapeutic alternative(s) do not meet the medical need of individuals with the disease or condition for an indication, as applicable.

FIELD	**RESPONSE FORMAT**
Response to Question 30	*Text* (1,000-word limit)
Additional Materials for Question 30	*Text* (Up to 50 citations; up to 10 tables/charts/graphs)

Does the evidence submitted include a cost-effectiveness measure:
[ ] Yes
[ ] No
[ ] Don't know

If yes to the question above, please select the applicable statement.
[ ] The evidence submitted includes QALYs or other cost-effectiveness measures that treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

[ ] The evidence submitted includes cost-effectiveness measures that DO NOT treat extending the life an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill.

Question 31: Patient and Caregiver Experience
Note: This question will be available only for respondents who indicate in Question 26 that they are a patient or caregiver.

Instructions for Question 31:

- For patients: Please describe your experience taking the selected drug and/or its therapeutic alternative(s).
- For caregivers: Please describe your experience and the experience of the person you care for that has taken the selected drug and/or its therapeutic alternative(s). When describing your experience as a caregiver, please focus on experiences that directly impact the health and wellbeing on the person you care for.

Questions on Patient and Caregiver Experience:

- What is your experience taking the selected drug and/or its therapeutic alternative(s)? How long have you been taking the selected drug and/or its therapeutic alternative(s)?
- How did treatment with the selected drug and/or its therapeutic alternative(s) impact your health, including your symptoms?
- Please describe any side effects that you have experienced, and the impact of these side effects have had on you.
- How did treatment with the selected drug and/or its therapeutic alternative(s) impact your quality of life and wellbeing?
- Have you had challenges accessing or taking the drug? For example, challenges affording the drug, gaining coverage through your health insurance, or taking the drug as prescribed.

FIELD	RESPONSE FORMAT
Response to Question 31	*Text* (2,000-word limit)

Question 32: Executive Summary
Note: This question is available to all respondents except individuals who indicate in Question 26 that they are a patient or caregiver.

Instructions for Question 32:

- Please provide an executive summary of the information submitted for Section I Questions 27-30.
- Citations and study summaries do not need to be included in this question.

FIELD	RESPONSE FORMAT
Response to Question 32	*Text* (1,000-word limit)

J. Certification of Submission of Section I for All Respondents

Required for All Respondents of Section I

Certification:
I certify that all information and statements made in this submission are true and current to the best of my knowledge and belief and are made in good faith. 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 payment purposes, including determination of a maximum fair price, as defined in section 1191(c)(3) of the Social Security Act.

Yes [ ]
No [ ]

Contact Information for respondent:

Field	**Response**
Name of the Person Responsible for the Submission	*Text*
Signature	*Text*
Date	*MMDDYYYY*

Paperwork Reduction Act Disclosure Statement:

According to the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number. The valid OMB control number for this information collection is **0938-XXXX (Expires XX/XX/XXXX)**. This contains both a mandatory and voluntary information collection. The time required to complete this information collection is estimated to average 2 hours for individuals and 20 hours for organizations per response for the general public and 500 total hours for the manufacturers of selected drugs, including the time to review instructions, search existing data resources, gather the data needed, and complete and review the information collection. If you have comments concerning the accuracy of the time estimate(s) or suggestions for improving this form, please write to: CMS, 7500 Security Boulevard, Attn: PRA Reports Clearance Officer, Mail Stop C4-26-05, Baltimore, Maryland 21244-1850.

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