

United States Food and Drug Administration
Assessment of Combination Product Review Practices
OMB Control No. 0910-NEW

SUPPORTING STATEMENT Part A. Justification

1. Circumstances Making the Collection of Information Necessary

Pursuant to the requirements of the Paperwork Reduction Act (44 USC 35) and Public Law, No. 115-52, 131 Stat. 1005 (also known as the Food and Drug Administration Reauthorization Act of 2017, or FDARA), the U.S. Food and Drug Administration (FDA) is requesting Office of Management and Budget (OMB) approval of the information collection that FDA committed to in Section I.I.5.g of the Prescription Drug User Fee Act (PDUFA) Reauthorization Performance Goals and Procedures Fiscal Years 2018 Through 2022 letter (“PDUFA VI Commitment Letter”). Section I.I.5.g of the PDUFA VI Commitment Letter states that an independent third party will assess current practices for combination product review, and that the contractor “will be expected to engage both FDA staff and individual sponsors as part of the assessment”.

In 1991, FDA’s Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), and Center for Devices and Radiological Health (CDRH) entered into “Intercenter Agreements” to provide guidance on the classification and assignment of medical products and to clarify jurisdiction over combination product reviews. With the enactment of the Medical Device User Fee and Modernization Act (MDUFMA) of 2002, FDA aimed to achieve prompt assignment of combination products, timely and effective premarket reviews, and consistent and appropriate postmarket regulation through the establishment of the Office of Combination Products (OCP). Since then, OCP has operated to further standardize combination product guidance to FDA and industry and facilitate coordination between FDA’s medical product review Centers. In 2017, as part of the sixth authorization of PDUFA, FDA committed to advance the development of drug-device and biologic-device combination products regulated by CDER and CBER through modernization of the combination product review program.

To meet this PDUFA VI commitment, FDA contracted with Eastern Research Group, Inc. (ERG) to assess current practices for combination product review. Assessment results will help FDA understand sponsor/applicant perspectives on what is working well, challenges and pain points, lessons learned, and opportunities for improvement in submissions and reviews for combination products. FDA will use assessment findings to inform potential updates to relevant documents, such as Manuals of Policies &

Procedures (MAPPs) and Standard Operation Procedures & Policies (SOPPs) for the review and submission of combination product applications.

In accordance with the PDUFA VI Commitment Letter, FDA proposes to have ERG conduct independent interviews with a sample of combination product sponsors who have submitted a Request For Designation (RFD), pre-Request For Designation (pre-RFD), Investigational New Drug (IND), or pre-Investigational New Drug (pre-IND) and applicants who receive a first-cycle action from FDA on a combination product New Drug Application (NDA) or Biologics License application (BLA). The purpose of these interviews is to collect feedback from combination product sponsors and applicants on their experience with FDA during the development and review of their products, including any challenges or best practices experienced. ERG will not ask sponsors/applicants for any confidential business information, nor will ERG ask applicants to evaluate the performance of FDA staff. Instead, interviews will focus on experiences with the combination product development and review process. Some sponsors/applicants might perceive their individual feedback about the review process to be sensitive given that they might interact with FDA about other products in the future. To address these potential concerns, ERG will not share any identifying information with FDA and will include only anonymized, aggregated interview results in the assessment report. FDA will publish ERG's assessment (with interview results and findings) on the Agency's public website.

The independent assessment, including information from combination product sponsor/applicant interviews, will be of great interest to FDA's stakeholders, including the regulated industry, patient and consumer groups, healthcare professionals, and Congress. Equally important, the assessment will be critical in determining whether and how to refine submission and review practices to advance development of combination products.

2. Purpose and Use of the Information Collection

FDA's contractor for the independent combination product review practices assessment has prepared a draft protocol and scripts for scheduling and conducting interviews with a sample of sponsors who submit combination product RFDs, pre-RFDs, INDs, and pre-INDs and with applicants who receive first review cycle actions from FDA on combination product NDAs and BLAs. Most of these respondents are private-sector companies; a few are education, non-profit, or government organizations. The protocols ensure that ERG is aware of all entities who are candidates for interviews and schedules and conducts interviews in a timely, consistent manner using good interview practices. The interview scripts include open-ended questions aimed at obtaining a thorough understanding of sponsor/applicant experiences and insights about review practices for their combination products.

The contractor will analyze open-ended responses to identify practices that sponsors perceive as helpful to the combination product development or review process as well as practices that might benefit from improvement. In addition, ERG will consider how interview responses might explain or provide context for results from other parts of the independent assessment, such as metrics pertaining to Inter-Center Consult Requests (ICCRs). In this way, ERG will use interview responses to complement and supplement data on combination product review parameters obtained through other means, such as extraction of data from FDA corporate databases and interviews with FDA review staff. ERG will synthesize and interpret the results to develop a set of findings and recommendations for combination product reviews to be included in the final assessment report.

In turn, FDA will use the independent assessment results, findings, and recommendations to:

- Determine the current state of combination product development and review practices.
- Determine whether and how to refine combination product review practices to reflect a modern landscape.
- Demonstrate compliance with the commitment to conduct and publish an independent assessment.
- Share information about combination product review practices with the regulated community, the public health community, Congress, and the general public.

3. Use of Improved Information Technology and Burden Reduction

FDA's contractor will not employ any web-based resources in soliciting combination product sponsor/applicant feedback. While online surveys can be distributed quickly and easily to a large volume of respondents, they are not the best vehicle for discussing the nuances of respondents' individual experiences, insights, and reasoning. Even surveys with open-ended questions do not permit immediate follow-up exchanges to clarify or elucidate responses; any follow-up requires additional contact with respondents, increasing burden. Interviews provide the more detailed and nuanced feedback needed for this independent assessment in a way that minimizes burden.

The contractor will minimize burden by offering to conduct interviews by telephone or videoconference if meeting in person is burdensome. Based on experience with previous PDUFA-related assessments, FDA estimates that 95% of respondents will opt for interviews by telephone or videoconference. FDA estimates that 5% of interview participants will participate in person because of their proximity to an interview location.

Finally, the interview instrument has been designed to elicit the desired feedback in as short an interview time as possible.

4. Efforts to Identify Duplication and Use of Similar Information

The information from combination product sponsors and applicants that FDA seeks is unique to this assessment and does not currently exist. FDA's contractor will request combination product sponsor/applicant feedback shortly after FDA reviews their submissions during the data collection period. No other known entities are collecting combination product-specific feedback on review practices during these stages of drug development. Furthermore, FDA is conducting this information collection in support of a commitment made to industry for PDUFA VI.

5. Impact on Small Businesses or Other Small Entities

FDA estimates that approximately 39% of interview respondents (about 187 individuals) will be employed by sponsors that are small businesses (where small business is defined as having up to 500 employees). The information being requested has been held to the absolute minimum required for the intended use of the data. In addition, FDA's contractor for the independent assessment will not ask small businesses or entities to travel, pay for telephone charges, or incur other unusual expenses. To avoid such expenses and minimize burden, ERG will conduct interviews by telephone if the sponsor/applicant chooses or will not be in or near Silver Spring, MD during the desired interview timeframe.

6. Consequences of Collecting the Information Less Frequently

FDA's contractor will ask interview respondents to participate in one interview per RFD/pre-RFD, IND/pre-IND, or NDA/BLA. This is the minimum frequency possible to obtain the required feedback from sponsors and applicants on their experiences with FDA review practices during combination product development review and application review.

To maximize respondent recall and minimize burden, FDA's contractor will ask combination product sponsors and applicants to discuss their experiences with submissions and review experiences shortly after they receive an FDA decision or action (i.e., RFD decision or pre-RFD assessment, IND decision or pre-IND assessment, or NDA/BLA first-cycle action).

There would be several consequences of not collecting the data as proposed. First, FDA would not fulfill its PDUFA VI commitment to conduct an independent assessment of combination product review practices with sponsor/applicant input. Second, FDA would lack sponsor/applicant perspectives on best practices and potential improvements for combination product reviews to help advance the development of combination products

during PDUFA VI. Finally, applicants would not have the opportunities they expect to share their opinions about the combination product review process.

The proposed data collection is a one time only.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances for the collection of information.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60-day notice for public comment in the FEDERAL REGISTER of 9/27/2018 (83 FR 48822). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

No incentives are being offered to respondents to participate in this information collection.

10. Assurance of Confidentiality Provided to Respondents

FDA has enlisted an independent contractor, ERG, to conduct the interviews that comprise this data collection. FDA staff will not participate in any surveys or interviews with sponsors and applicants. In addition, ERG will keep individual respondent information private by: (1) handling all information processing internally; (2) securely storing raw interview information; and (3) sharing only anonymized aggregated summaries of results with FDA and the public.

FDA maintains its own data on RFDs/pre-RFDs, INDs/pre-INDs, NDAs/BLAs, and their associated sponsors and applicants. Therefore, the agency will know what sponsor/applicant organizations could be asked to participate in interviews for this project. FDA will not know which organizations—or which individuals employed by these organizations—responded to interview requests.

While there is no express assurance of confidentiality that can be supported by law, the design of the data collection will allow responses to be anonymous. Interviewees will be assured of the privacy, to the extent available under law, of their responses through language placed prominently on all interview materials as well as introductory comments made by the interviewer. ERG will assure respondents of the privacy of their information by incorporating the following text into survey instruments and interview scripts:

“Your participation / nonparticipation is completely voluntary and your responses will not have an effect on your eligibility for receipt of any FDA

services. In instances where respondent identity is needed (e.g., for follow-up of non-respondents), this information collection fully complies with all aspects of the Privacy Act and data will be kept private to the fullest extent allowed by law.”

Interviewers will be trained on the privacy of responses and will be prepared to describe the policy in detail, provide examples, and respond to any related questions from participants. For example, the interviewer will explain that each individual’s answers will be combined with those of others and presented in summary form only, and that FDA will not have access to the names of participants.

This information collection does not involve collection of personally identifiable information (PII). This project does not require Institutional Review Board (IRB) review because this assessment does not constitute biomedical research on human subjects.

11. Justification for Sensitive Questions

No sensitive questions will be asked of respondents during this information collection. Some interview questions ask applicants for frank assessments of the combination product development and review process, which might be perceived as sensitive to some applicants. This information is crucial to understanding the current state of FDA and sponsor practices in combination product development and review, what practices contribute to efficient review, and what practices can be refined to improve review coordination. The contractor will keep private the identity of individual applicants, as well as each applicant’s responses to interview questions; all interview materials will emphasize this. No individual applicant will be identified as an interviewee to FDA.

12. Estimates of Annualized Burden Hours and Costs

12 a. Annualized Hour Burden Estimate

Estimated participation times are based on experience with similar interviews for similar types of PDUFA-related assessment projects. Combination product sponsors and applicants will participate in interviews via teleconference or, if convenient, face-to-face meeting; interview questions are attached. The time required to respond to requests for an interview and participate in the interview is estimated to be 90 minutes.

Table 1. Estimated annual reporting burden

Portion of Study	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Pre-test	5	1	5	1.5	7.5
Interviews	339	1	339	1.5	508.5
Total					516

¹There are no capital costs or operating costs associated with this collection of information.

12b. Annualized Cost Burden Estimate

FDA estimates the annualized cost to respondents to be the burden hours estimate multiplied by the median hourly wage estimate (Source: Occupational Employment Statistics, Bureau of Labor Statistics). FDA used the median wage estimate (\$90.00) for Physicians and Surgeons, All Others, Standard Occupational Code (SOC) 29-1069, because this wage falls in the middle of the range of wages for NDA/BLA managers in the pharmaceutical industry. FDA multiplied this median wage by 1.4 to capture benefits, resulting in a loaded hourly median wage rate of \$126.00.

Table 2. Annualized cost to respondents.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
RFD/Pre-RFD Sponsors	159	\$126.00	\$20,034.00
IND/Pre-IND Sponsors	213	\$126.00	\$26,838.00
NME NDA / Original BLA Sponsors	137	\$126.00	\$17,262.00

The total annualized cost to respondents (across the three types of respondents) is \$64,134.00.

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

This 2-year independent assessment of combination product review practices encompasses several evaluation methodologies, including interviews with sponsors/applicants for combination product RFDs/pre-RFDs, INDs/pre-INDs, and NDAs/BLAs. The interview effort involves development of an interview protocol and script, implementation of the interviews, and analysis of results to develop findings and recommendations about combination product review practices. The annualized cost to the Federal government is estimated to be \$135,000, which is the total contractor cost and FDA oversight cost of the interview portion of the independent assessment project: approximately \$8,000 is for interview development costs (e.g., instrument development, implementation design, etc.), \$117,000 is for interview implementation and analysis, and \$10,000 is for FDA oversight of contractor activities. There are no other costs to the Federal government for implementation.

15. Explanation for Program Changes or Adjustments

This is a new data collection.

16. Plans for Tabulation and Publication and Project Time Schedule

The contractor conducting the independent assessment will present results, including interview results, in a single report titled “Assessment of Combination Product Review Practices: Final Report”.

FDA will publish this report on the FDA’s public website.

Table 3. Schedule for project tasks.

Tasks	Schedule
Draft interview protocols and scripts	July 9, 2018
Finalize interview protocols and scripts	After public comment on 60-day notice for ICR
Conduct interviews	February 1, 2019 through August 31, 2020
Analyze interview information	Quarterly
Prepare initial assessment report	April 13, 2020
Publish final report	September 30, 2020

17. Reason(s) Display of OMB Expiration Date is Inappropriate

FDA will display the OMB expiration date as required by CFR 1320.5.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.