ASSESSMENT OF COMMUNICATION THROUGH PRODUCT QUALITY INFORMATION REQUESTS DURING APPLICATION REVIEW

Statement of Work

Food and Drug Administration (FDA)

I. BACKGROUND

The Prescription Drug User Fee Act (PDUFA) provides FDA with a source of stable, consistent funding that has made it possible for the Agency to focus on promoting innovative therapies and help bring to market critical products for patients. When PDUFA was originally authorized in 1992, it had a five-year term. The program has been subsequently reauthorized every five years. To prepare for reauthorization of PDUFA for the next five-year period (2023 to 2027), FDA conducted negotiations with the regulated industry and held regular consultations with public stakeholders including patient advocates, consumer advocates, and healthcare professionals between September 2020 and February 2021.

Following these discussions, related public meetings, and Agency requests for public comment, FDA published the "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027" document, also known as the PDUFA VII "goals letter", to supplement the statute. The goals letter includes the performance goals, procedures, and commitments that apply to aspects of the human drug review program that are important for facilitating timely access to safe, effective, and innovative new medicines for patients. Several of these commitments aim to continue to enhance communication between FDA and sponsors during application review.

Communication Between FDA and Sponsors During Application Review

FDA and sponsors interact in a variety of ways throughout application review. One such way is via a communication, called an information request (IR), sent to an applicant as the discipline review occurs. FDA uses IRs to request further information or clarification that is needed or would be helpful to allow completion of the discipline review.[1] IRs may be in the form of letters, emails, or fax. [2]

FDA uses product quality IRs to request further information or clarification needed for FDA's assessment of identity, strength, quality, purity, or potency of drug substances or drug products.[3] Ensuring that patients can have confidence in the safety and effectiveness of their

[1] Guidance for Industry: Information Request and Discipline Review Letters Under the Prescription Drug User Fee Act (November 2001). https://www.fda.gov/media/77409/download
[2] CBER SOPP 8401.1: Issuance of and Review of Responses to Information Request Communications to Pending Applications (December 2020). https://www.fda.gov/media/85301/download
[3] Internal MAPP 5016.8: Communication Guidelines for Quality-Related Information Requests and Deficiencies

medications is a longstanding priority for FDA. The Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) have worked to address this priority, in part, by performing Chemistry, Manufacturing, and Controls (CMC) reviews for CDER- and CBER-regulated products. CDER or CBER may issue a product quality, or CMC, IR as a result of CMC assessments conducted in support of the application.

Enhancements Related to Product Quality Reviews, Chemistry, Manufacturing, and Controls Approaches

IRs from both CDER and CBER are expected to follow Four-Part Harmony in which reviewers are expected to communicate (i) what was provided, (ii) what is the issue or deficiency, (iii) what is needed, and (iv) why it is needed. This expectation can be found in the internal CDER MAPP 5016.8, *Communication Guidelines for Quality-Related Information Requests and Deficiencies*. As a result of FDA's implementation of Four-Part Harmony in CMC-IRs, sponsors should understand what information FDA needs to continue their review.

During PDUFA negotiations, based upon discussions with industry, it appeared that there may be an inconsistent use of Four-Part Harmony in CDER and CBER information request letters. To address this, the PDUFA VII goals letter includes commitments for FDA to update and conduct training on existing policies and procedures (MAPPs and SOPPs), related to Four-Part Harmony. CDER MAPP 5016.8, *Communication Guidelines for Quality-Related Information Requests and Deficiencies* will be revised and made public. CBER SOPP 8401.1, *Issuance of and Review of Responses to Information Request Communications to Pending Applications* will also be revised.

In addition to updating the documents and conducting training, FDA committed to contracting with an independent third party to assess current practices of CDER, CBER and sponsors in communicating through product quality IRs during application review and effectiveness of Four-Part Harmony. This assessment will identify best practices and areas of improvement in communications between FDA review staff[4] and sponsors through product quality IRs and is the subject of this task order.[5]

II. OBJECTIVES

The primary objectives of this assessment are to assess the effectiveness of Four-Part Harmony and identify best practices and areas for improvement in communication between FDA review staff and sponsors through product quality IRs. This involves assessing trends across IRs and application of Four-Part Harmony as described in CDER MAPPs and CBER SOPPs.

[4] For the purposes of this SOW, consistency with the PDUFA goals letter, "FDA review staff" refers to staff within CDER and CBER.
[5] PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027. https://www.fda.gov/media/151712/download

Key Objectives

Using information from both qualitative data gathered from interviews and FDA's corporate databases as well as other databases (e.g., database or other tracking mechanism developed by the contractor):

1. Characterize and analyze trends across the baseline state of communication between FDA review teams and sponsors via product quality IRs, before the implementation of PDUFA VII commitments (i.e., updating MAPPs and SOPPs and conducting training).
2. Characterize and analyze trends across the current state of communication between FDA review teams and sponsors via product quality IRs, after implementation of PDUFA VII commitments, as compared to the baseline, expectations of FDA and sponsors, and the practices stated in relevant FDA MAPPs and SOPPs.
3. Identify what is working well and what is not working well with the current status of product quality IR communication after implementation of PDUFA VII commitment; this includes identifying best practices and areas for improvement.
4. Make recommendations for both FDA review staff and sponsors on how to improve communications via product quality IRs.

III. SCOPE OF WORK

This project will assess the quality and alignment of product quality IRs with updated FDA MAPPs and SOPPs related to Four-Part Harmony, as well as the effectiveness of Four-Part Harmony overall. The project will also assess if IRs are appropriate for what FDA and sponsors expect in an application. The scope of this contract will cover all aspects of data collection, analysis, assessment, interviewing key FDA staff and sponsors, reporting, documentation, and other tasks deemed necessary to conduct a thorough assessment of product quality IRs.

The assessment will cover product quality-related IRs associated with original new drug applications (NDAs) and biologics licensing applications (BLAs) (excluding biosimilar BLAs submitted under 351(k) of the Public Health Service Act) and their amendments[6] during the first cycle of review by CDER and/or CBER. IRs and amendments associated with supplements or multiple review cycles are out of scope. Given the high volume of IRs, the assessment will be based on two samples of applications and their associated product quality IRs and amendments – a baseline sample and a current sample (the study cohort). The study cohort will be balanced across CDER and CBER, proportional to the number of applications received by each Center.

The contractor shall use the sample characteristics noted below, as well as any others that the Project Advisory Group (PAG) may recommend, to design the study cohort:

- Application type (i.e., NDA or BLA)
- Review priority (e.g., priority, standard)
- Therapeutic area
- Date of last action – baseline only

[6] Amendments are additional data or analysis submitted by an applicant after original submission of an application.

- Submission status (e.g., approved, pending) – baseline only

FDA expects that the study cohort will include roughly 80 applications (~40 for the baseline and current samples each). FDA estimates that there are roughly 5 product quality IRs per application and 7 product quality amendments per application.[7] The contractor should work closely with the PAG in designing the study cohort to ensure a representative sample.

The contractor shall collect quantitative and qualitative data on the state of product quality IRs in the study cohort using a mixed methods approach. This approach will include analyzing IRs housed in corporate databases and conducting contractor-led interviews with FDA review staff and sponsors, as well as any other methods the contractor and PAG agree upon. FDA does not expect that the contractor will conduct interviews or surveys about the baseline sample, although the contractor may include interview questions to FDA staff and sponsors about their experience with IRs in the past.

The contractor will be responsible for developing interview guides and data collection tools to collect qualitative and quantitative data on the state of product quality IRs. Specific metrics and interview questions should be developed by the contractor, in consultation with the FDA PAG, using relevant guidances[8] and the aforementioned MAPPs and SOPPs as source documents to assess quality and alignment of IRs. In some cases, the contractor may want to use performance metrics that are concurrently collected by FDA to augment their own analyses. The contractor should consider, but not be limited to, the following characteristics of product quality IRs to inform interview questions and quantitative metrics:

- Number of product quality IRs and amendments per application
- Division sending the IR and associated content
- Compliance of the IR with Four-Part Harmony as described in revised CDER and CBER MAPPs and SOPPs
- Nature and type of the question or issue identified in the IR, relative to the goal date
- FDA and sponsor expectations of content submitted with an application
- Sponsor understanding of FDA's requests in IRs (i.e., clarity of the IR)
- FDA and sponsor characterization of IR quality
- Trends in IRs across sample characteristics
- Overall FDA and sponsor perspectives on challenges and best practices with IRs

As specified in the PDUFA VII goals letter, the contractor shall describe their findings and recommendations in a final report, to be published for public comment no later than June 30, 2025. The final report is detailed in task 11 of the following section.

[7] Estimates based on NDA and BLA applications for which a review action was taken during fiscal years 2018-2020.
[8] Note: Relevant guidances include those that describe the process for communications between FDA and applicants. The scientific and technical content of IRs is out of scope.

IV. TASKS

Project Initiation

1. The contractor shall participate in a project kick-off meeting to review the task order, including the project timeline, scope, and schedule of deliverables. At this meeting, the contractor shall present its proposed overall approach and work plan to the FDA PAG. The contractor shall revise the proposed approach based on FDA feedback.

2. The contractor shall participate in an orientation period to become familiar with the details of FDA's quality review and IR processes, relevant guidances/MAPPs/SOPPs, obtain access to all necessary IT systems, and attend any necessary and relevant FDA trainings. This orientation period will last about two weeks.

3. The contractor shall develop a detailed evaluation plan to assess the study cohort of product quality IRs. The evaluation plan shall include a sampling framework for identifying the applications to be included in the baseline and current samples, methods for identifying interviewees for the current sample, a list of metrics based on the Objectives and Scope of Work, and a quantitative and qualitative approach to collecting and analyzing data to meet the Objectives. The evaluation plan shall also include the contractor's plans for oversight and communication during the assessment. The contractor shall present the evaluation plan to FDA and revise the plan based on FDA feedback.

4. The contractor shall develop the necessary tools (e.g., data collection instruments, interview guides, survey questions, databases) for capturing and analyzing information collected in accordance with the assessment approach. The data collection instruments, interview guides, and other tracking tools shall be modified as necessary throughout the assessment based on accumulated experience. The qualitative data tools should include inquiries that elicit current and prior best practices and challenges of both sponsors and FDA, as well as FDA and sponsor perspectives on the quality and clarity of IRs over time. The contractor shall present the tools to FDA and revise the tools based on FDA feedback.

5. The contractor shall develop a proposed approach to the quantitative and qualitative analysis of all data collected for the assessment. The contractor shall present the proposed approach to FDA and subsequently revise it based on any FDA feedback.

6. The contractor shall prepare all necessary materials for the Office of Management and Budget (OMB) approval for data collection materials that will be facilitated by the FDA project manager and staff. The Paperwork Reduction Act (PRA) requires the FDA to

follow and complete HHS and OMB approval processes and procedures for federally sponsored data collections.[9]

Project Execution

7. The contractor shall execute data collection in accordance with the finalized evaluation plan and its methods and metrics, which are to include but not be limited to:
    a. Assessing application of all relevant past and current guidances/MAPPs/SOPPs and other documents or activities that guide or have guided FDA practice in preparing product quality IRs.
    b. Retrieving and reviewing all relevant documentation related to the applications and corresponding IRs and amendments included in the study cohort.
    c. Scheduling and conducting independent interviews of FDA review staff and sponsors relevant to applications included in the current sample. The total number of interviews will be based on the number of applications selected as part of the current sample and will not total more than 100. The contractor shall conduct interviews with members of each selected application's review team from product quality disciplines and the sponsor. The contractor shall manage the process of inviting and scheduling all interviews. The contractor shall use the interview guide(s) developed in task 4. The information shall be aggregated and made anonymous prior to inclusion in any report, including reports to the PAG.

8. Using quantitative and qualitative data collected, the contractor shall conduct an analysis in accordance with the evaluation plan to assess the stated objectives. The conduct of the analysis shall be ongoing, culminating in a final assessment of the state of current product quality IRs. Analysis of the current sample should include but not be limited to:
    a. Descriptive analysis of the data collected
    b. Comparisons across sample characteristics
    c. Comparisons across the baseline and current sample
    d. Comparisons across each sample and relevant FDA guidance/MAPPs/SOPPs
    e. Qualitative analysis of FDA and sponsor interviews and survey responses (if applicable)
    f. Recommendations to improve and/or modify product quality IR practices

9. Throughout the assessment, the contractor shall also account for current ongoing initiatives and pilot programs that the Agency is undergoing to address previously or internally identified issues, as these may affect the findings of the assessment over time.

Project Reporting

10. The contractor shall brief the FDA Project Manager every two weeks.

[9] More information for the PRA and data collection procedures can be found here: https://www.hhs.gov/ocio/policy/collection/infocollectfaq.html

11. The contractor shall present an interim analysis summary to the FDA PAG in the third quarter of fiscal year 2024. The presentation shall include the status of data collection and analysis and early insights from the data analysis.

12. The contractor shall complete a final analysis and develop a final report summarizing the assessment methodology, data, analysis, key learnings, and recommendations. The contractor shall submit to FDA a draft of the final assessment report by January 30, 2025. The contractor shall also present the draft final assessment to the FDA PAG. The contractor shall subsequently revise the draft based on FDA feedback by March 31, 2025. The final report shall be published on FDA's website by June 30, 2025.

13. The contractor shall prepare a Federal Register Notice to request public comment on the final report. The contractor shall support the FDA Project Manager through clearance and posting of the Federal Register Notice by tracking the process and making revisions.

General Administrative Tasks

14. The contractor shall take meeting minutes at all project-related updates and meetings with the PAG and any other FDA stakeholders and provide final meeting minutes to the FDA Project Manager within 2 business days.

15. The contractor shall develop and send all project-related slides or other documents pertinent to any project meeting, such as project updates or final briefings, to the FDA Project Manager 2 business days in advance.

In addition to the deliverable formats described in the following section, the final report shall be submitted in Adobe Acrobat portable document format, compliant with Section 508 of the Rehabilitation Act and suitable for posting on FDA's website. The posted version of the assessment shall be redacted as appropriate to protect commercial confidential information.

V. DELIVERY

The scope of work forms the basis for the following proposed schedule of deliverables. The actual schedule of deliverables may vary based on the final agreed-upon evaluation plan, which should conform to the PDUFA VII commitment of FDA publishing a final report by June 30, 2025. All documents, plans, diagrams, presentations, etc. are to be submitted solely in electronic form and in the native file format of Microsoft Word 2003, Excel 2003, or Power Point 2003, or later versions. The task number corresponds to the tasks described in section IV. The deliverable number is unique to the deliverable. The contractor shall provide the following, as a result of specific tasking in performance of the activities in this SOW:

Task #	Requirement	Expected Media	Deliverable #	Target completion timeline or frequency of deliverable
Project Initiation				
1	Draft overall approach and work plan	PowerPoint presentation & Word document	1a	1 week after award
1	Revised overall approach and work plan	PowerPoint presentation & Word document	1b	3 weeks after initiation
3	Draft evaluation plan including a sampling framework, methods for identifying interviewees, metrics, analysis approach, and oversight and communications plans	PowerPoint presentation & Word document	2a	5 weeks after initiation
3	Revised evaluation plan	Word document	2b	8 weeks after initiation
4	Necessary tools for capturing and analyzing information collected in accordance with the assessment approach	Word documents, Excel files, etc. as applicable to the tools	3a	11 weeks after initiation
4	Revised necessary tools for capturing and analyzing information collected in accordance with the assessment approach	Word documents, Excel files, etc. as applicable to the tools	3b	14 weeks after initiation
5	Draft approach to quantitative and qualitative analysis of data collected	Word document(s)	4a	15 weeks after initiation
5	Revised approach to quantitative and qualitative analysis of data collected	Word document(s)	4b	18 weeks after initiation
6	Necessary materials for OMB approval of data collection materials	Word document(s)	5	Beginning 7 weeks after initiation, as needed
Project Reporting				
10	Briefings with the FDA Project Manager	PowerPoint presentations	6	Every two weeks
11	Interim analysis summary	PowerPoint presentation	7	April-June 2024

12	Draft final assessment report	PowerPoint presentation & Word document	8a	January 30, 2025
12	Revised final assessment report	Word document	8b	March 31, 2025
13	Draft Federal Register Notice to request public comment on the final report	Word document	9	March 31, 2025
General Administrative Tasks				
14	Meeting minutes for project-related updates and meetings with the PAG and any other FDA stakeholders	Word document	10	Within 2 business days of the relevant meeting

VI. STAFFING

The contractor shall staff the project with one project manager or analyst who shall be responsible for participating in kick-off/closing meetings, ensuring that personnel are making necessary progress in meeting deliverable deadlines, holding regular progress updates with FDA, resolving any performance issues with personnel, and contributing to the qualitative and quantitative data gathering and analysis, among other duties. FDA expects that this task order will require contribution by at least one senior program evaluation subject matter expert with expert knowledge of qualitative and qualitative research and analysis and program evaluation. In addition, FDA expects the project to be staffed with at least two entry-level or junior program evaluation subject matter experts with experience in qualitative and quantitative data gathering and analysis.

VII. GOVERNMENT FURNISHED PROPERTY

The FDA will provide laptops, badges, network access, and access to relevant FDA data systems to all contractors. FDA badges and government furnished equipment will be provided to the contractor within one month following the date of award. Immediately after award of the contract, the contractor will provide a complete list of all personnel to FDA.

VIII. PERIOD OF PERFORMANCE

Performance of this task order shall commence on the task order execution date and shall not extend beyond June 30, 2025. The estimated period of performance is 24 months.

IX. SECURITY AND PRIVACY

The contractor agrees that contractor personnel will not divulge, or release data or information developed or obtained in connection with the performance of the resulting contract, unless made public by FDA or upon written approval of the Government.

Except as may otherwise be permitted by a data owner, the contractor personnel agree not to use, disclose or reproduce proprietary data, other than as required in performance of the contact; provided, however, that nothing herein shall be construed as precluding the use of any data independently acquired by the contractor without such limitation.

Due to the sensitive nature of the information involved, all contractor personnel will be required to sign a non-disclosure agreement before data and information otherwise exempt from public disclosure (e.g., Privacy Act or Data Collected Under an assurance of Confidentiality) may be disclosed to them.

The contractor shall submit a roster, by name, position and responsibility, of all staff (including subcontractor staff) working under the contract that will develop, have the ability to access, or host and/or maintain a Federal information system(s). The roster shall be submitted to the Project Officer, with a copy to the Contracting Officer, within 14 calendar days of the effective date of the contract. Any revisions to the roster as a result of staffing changes shall be submitted within 15 calendar days of the change.

Each contractor/subcontractor employee who may have access to non-public Department information under this contract shall complete and submit the FDA Form 3398: Contractor's Commitment to Protect Non-Public Information (NPI) Agreement available upon request from the FDA Intranet site. A copy of each signed and witnessed Non-Disclosure agreement shall be submitted to the Project Officer or designee prior to performing any work under the contract. The Project officer or designee will inform the contractor of any additional forms and training that are required.

X. PLACE OF PERFORMANCE AND EQUIPMENT

Per current COVID-19 restrictions, the contractor will work entirely virtually, until otherwise notified. Contract-related technical work may be performed off-site via Virtual Private Network (VPN) using FDA-issued laptops/computer equipment with tokens, personal identity verification (PIV) cards (badges) and appropriate network accounts. The contractor shall be responsible for providing internet access, so contractor-assigned computers are able to connect to the FDA network via VPN. Should COVID-19 restrictions change, the contractor may report to FDA's White Oak Headquarters, located at 10903 New Hampshire Avenue, Silver Spring, MD 20993.

FDA provides laptops and badges, as necessary for access to relevant FDA data systems. These materials and resources shall remain the property of the US Government and shall be returned in good condition to the COR at the conclusion of the period of performance.

Otherwise, the contractor will be responsible for providing their own equipment. FDA badges and Government furnished equipment will be provided to the contractor within one month following the date of award. For activities requiring on-site participation, FDA will provide the contractor with workspace as necessary on the White Oak campus. The contractor may be required to utilize hoteling space, existing offices, or other shared space at the campus and move frequently while working at the White Oak Campus.

XI. EVALUATION CRITERIA

The following evaluation criteria will be used in assessing the technical proposals for the work specified in this statement of work:

1. **Factor 1: Technical Plan / Approach:** The Government will evaluate the extent to which the Offeror's proposal demonstrates:

    - The level of knowledge and understanding of the technical requirements and the tasks to be performed
    - An understanding of the required scope of each task
    - The ability to efficiently and effectively elicit feedback from subject matter experts
    - The ability to effectively use Microsoft Excel, Access, and SharePoint tools with minimal training and guidance

2. **Factor 2: Personnel / Relevant Experience:** The Government will evaluate the extent to which the Offeror's proposal demonstrates:

- The ability to provide qualified and experienced personnel relevant to the task requirements. FDA will place particular emphasis on evaluating the expertise and experience in evaluation, conducting interviews, and mixed methods analysis.
- Relevant experience and performance under existing and prior contracts for similar products or services. Performance information shall be used as an evaluation factor against which contractors' relative rankings shall be compared to assure best value to the government. The government shall focus on information that demonstrates quality of performance relative to the size and complexity of the procurement under consideration.