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Handling Health Regulatory Information Requests: Best Practices and Strategies

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ABSTRACT

Addressing Information Requests (IRs) from health regulatory agencies such as FDA, EMA, MHRA, PMDA, etc., is critical during clinical trials. These agencies send information requests (IRs) for clarification, additional information, or verification of the data collected during the trial. For statistical programmers, responding to these IRs requires a detailed, step-by-step process, including information collection, resources and timeline planning, validation activities, maintaining documentation, and tracking all requests. This paper explores the statistical programming team's roles in handling IRs, exploring best practices and strategies for ensuring accuracy, efficiency, and compliance throughout the IR process, from information gathering to final submission. It helps programmers understand the technical and procedural aspects of information requests (IRs) and provides insight into navigating the best practices and strategies to enhance productivity and accuracy.

INTRODUCTION

Clinical trials provide the evidence needed to assess the safety and efficacy of the new drug. As the trial progresses and meets the defined endpoints for the study, sponsors submit the package to health regulatory agencies, such as the FDA, EMA, MHRA, PMDA, etc., to get new drug approvals. The key role of the regulatory agencies is to evaluate the safety and efficacy of the data submitted by the sponsors and its outcome. In many cases, health agencies issue information requests (IRs), which are formal inquiries seeking additional data, analysis, or clarification from sponsors.

The sponsor typically receives information requests at critical clinical trial stages, especially after regulatory submissions, during the inspection, or the post-inspection review. These requests address questions related to trial design, data integrity, statistical methodologies, and safety concerns. Information requests are important for ensuring transparency and compliance; they often create a tight timeline and require a quick and well-coordinated response from multiple functional groups.

IRs pose significant challenges and responsibilities for statistical programmers. Their role involves collecting information, evaluating work scope, conducting a new or supplemental analysis, managing resources, conducting validation activities, and tracking all requests. Additionally, statistical programmers are responsible for documenting their work to ensure traceability and reproducibility and coordinating with regulatory teams to meet the response deadline.

This paper provides details of how programmers can manage information requests effectively. It focuses on four critical aspects: gathering information, resources and timeline management, planning validation activities, and tracking and submitting IR responses. This paper guides best practices and strategies for statistical programmers navigating simple or complex information requests.

GATHERING INFORMATION

Gathering and understanding the requested information is the first and most important step in responding to a regulatory agency's Information Requests (IRs). Due to the IR's time-sensitive nature, it is crucial to have an efficient way to retrieve the information. Statistical programmers must work closely with cross-functional teams to understand the request, find the relevant data sources, extract the data (if required), and ensure they meet the regulatory requirements. The following chart displays the efficient approach to gathering information for the IR.

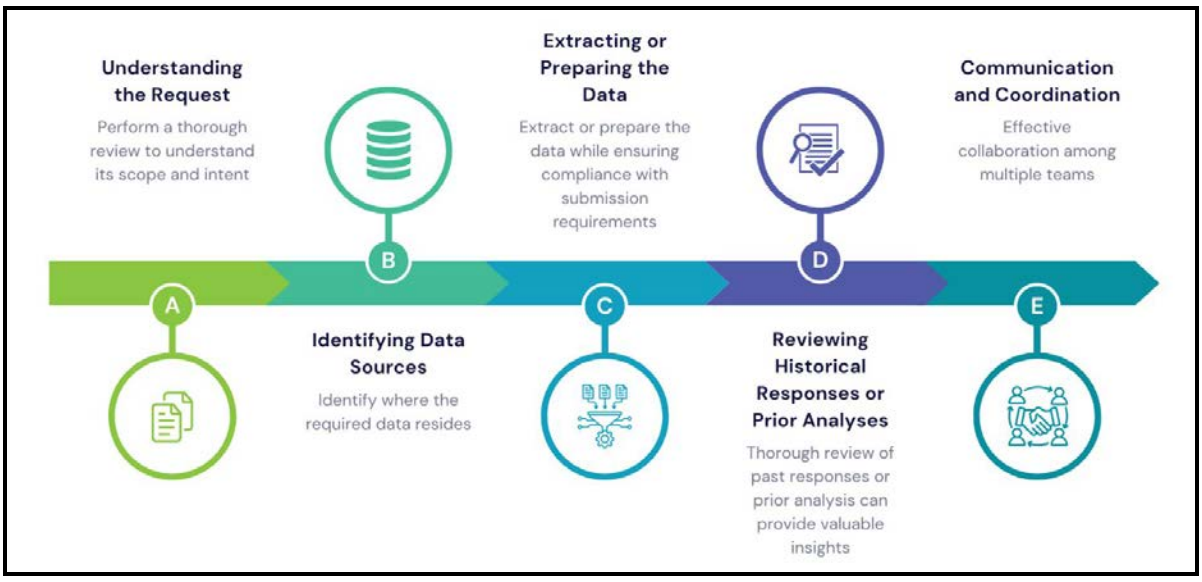

Figure 1. Information Gathering Approach for Information Requests (IRs)

The following section provides high-level information on each approach described in the above figure, with examples where applicable. The approach can be adjusted or modified based on the requirements, as not all IRs are the same in nature.

UNDERSTANDING THE REQUEST

When an IR is received, the first step is to perform a thorough review to understand its scope and intent. The programming team must carefully analyze the language and specific requirements outlined in the request to avoid misinterpretation. It includes identifying the following:

- **Type of Request**
  - Simple clarifications (e.g., confirming a specific dataset variable or population).
  - Additional statistical analyses (e.g., new subgroup analyses or sensitivity analyses).
  - Comprehensive explanations of methodologies used in analyses (e.g., rationale for statistical methods).
- **Key variables and data elements requirements**
  - Identifying specific datasets (e.g., SDTM, ADaM).
  - Assessing whether existing variables need to be modified or new variables need to be derived.
- **Regulatory context**
  - Understanding if the IR is a follow-up to a previously submitted response.
  - Reviewing guidance documents from agencies such as the FDA, EMA, and PMDA to ensure compliance and expectations.
- **Clarifications with regulatory and biostatistics teams**
  - If any aspect of the request is unclear, immediate communication with the regulatory or biostatistics teams is essential.
  - A regulatory expert may provide insights into how similar IRs have been handled in past submissions.

IDENTIFYING DATA SOURCES

Once the request is understood, the next step is identifying where the required data resides. Statistical programmers should:

- **Determine the relevant clinical datasets**
  - SDTM (Study Data Tabulation Model): If the request involves collected data, SDTM datasets should be referenced.
  - ADaM (Analysis Data Model): If the request involves statistical analyses, ADaM datasets will likely be the primary source.
- **Check the traceability of data**
  - If the IR requests specific patient data or derived endpoints, programmers should ensure proper traceability from SDTM to ADaM to TLFs (Tables, Listings, and Figures).
  - Reviewing metadata and dataset specifications can help to understand what's already available, what's missing, and what needs to be derived.
- **Identify external or supplemental data sources.**
  - IR requests related to safety data may require the use of integrated datasets (e.g., Integrated Summary of Safety (ISS) or Integrated Summary of Efficacy (ISE)), which are commonly developed for NDA submissions.
  - For the IR related to pharmacokinetic/pharmacodynamic (PK/PD) analysis, create an ADaM dataset for PK/PD data.
- **Review data quality and integrity**
  - Assess if any data issues exist that could impact response accuracy.
  - Communicate with data management in case of missing values, inconsistencies, or discrepancies that need resolution before responding to the IR.

EXTRACTING OR PREPARING THE DATA

After identifying the necessary datasets, statistical programmers may need to extract or prepare the data efficiently while ensuring compliance with submission requirements. Key steps in this process are filtering datasets and generating relevant data subsets needed for the analysis using SAS® or other statistical programming tools. The data selection must align with the request's specifications, particularly when selecting populations or data points per the IR.

Once the data has been extracted, the next step is to standardize it for submission. The standardization involves ensuring that the format of the extracted datasets matches the required submission format, such as adhering to CDISC standards. Additionally, programmers must follow regulatory guidelines regarding dataset structure, naming conventions, and documentation.

In some cases, programmers may need to create new datasets or modify derivations in existing datasets, depending on the requirements set forth by the IR. If the request calls for an analysis that was not originally planned, statistical programmers must create new datasets accordingly. Furthermore, if modifications to existing variable derivations are necessary, it is essential to document these changes and their reasons in the reviewer's guide.

REVIEWING HISTORICAL RESPONSES OR PRIOR ANALYSES

Regulatory agencies often issue Information Requests (IRs) related to previously submitted data or analyses. A thorough review of past responses can provide valuable insights into how to address the current IR effectively. This approach enhances the response's quality and demonstrates a commitment to transparency and thoroughness.

Checking previous submissions is essential to ensure a comprehensive response. This involves reviewing prior submission documents such as Clinical Study Reports, Data Reviewer's Guides, and Regulatory Response Packages. Organizations can maintain credibility with regulatory agencies by ensuring consistency between past and current responses, which fosters trust and facilitates smoother interactions.

Additionally, aligning with previously conducted analyses is crucial, and it can be achieved by comparing newly extracted datasets and analyses with those that were previously submitted. Identifying discrepancies and documenting the reasons for any differences will help clarify the regulatory agency's context and support the overall integrity of the submission.

COMMUNICATION AND COORDINATION

The success of an IR response depends on effective collaboration among multiple teams. One important team is Biostatistics, which plays a crucial role in confirming that the statistical methods align with the IR's intent. Their expertise ensures that the data analysis is appropriate and robust.

Another key team is Regulatory Affairs. This team is responsible for ensuring that the responses align with agency expectations and regulatory precedent. Their insight helps navigate the complexities of regulatory requirements. Clinical and Medical Writing teams also contribute significantly by verifying the clinical relevance and accuracy of the patient data. Their careful documentation ensures that the presented information is clear and scientifically valid, which is essential for the IR process. Additionally, Data Management is vital in resolving data inconsistencies or missing information, as accurate and complete data is fundamental to any successful response.

Regular meetings and clear documentation of discussions and decisions are essential to facilitate this collaborative effort. Such practices can help streamline the IR process and reduce turnaround time, leading to more efficient and effective response.

RESOURCES AND TIMELINE MANAGEMENT

Efficient resource planning is essential for responding to regulatory Information Requests (IRs) promptly and accurately. Since IRs often come with strict deadlines, statistical programmers must ensure that all experienced resources are appropriately allocated and coordinated. A structured approach to resource planning and timeline management helps minimize delays, reduces errors, and improves the overall quality of the response. The following approach may help effectively plan resources and set realistic timelines for IR response.

ASSESSING THE SCOPE OF THE REQUEST

Before planning resources for Information Requests (IRs), it is essential to assess the complexity and scope of the request. It involves categorizing the IR into three distinct types. Minor requests typically involve simple clarifications or minor adjustments to datasets, such as clarifying variable names and resubmitting a dataset. Moderate requests require additional analysis, the creation of new derived datasets, or providing explanations regarding statistical methodologies. In contrast, complex requests demand extensive re-analyses, multiple datasets integration, or responses requiring involvement from several functional teams.

Understanding regulatory deadlines is also a crucial aspect of this assessment process, as IR deadlines can vary significantly depending on the agency and the type of request. The typical timeline for responding to regulatory agency IRs is 10-14 calendar days, while the more time-sensitive requests timeline may be shorter (as little as 5–7 calendar days). Therefore, it is vital to prioritize urgent IRs immediately to ensure they meet submission deadlines. Additionally, identifying dependencies early on is important for efficient workflow management. It may involve waiting for updated datasets from data management and obtaining input from biostatisticians and the clinical and medical writing team.

ALLOCATION OF RESOURCES

Once the scope of the IR is assessed, the next step involves allocating resources appropriately. A well-defined team structure is essential to ensure that the right expertise is assigned to each response. Key

personnel typically include a lead statistical programmer, who oversees the programming aspects of the IR and coordinates with other programmers, statisticians, and regulatory teams to ensure compliance with submission standards. Statistical programmers are responsible for dataset extraction, enrichment, program development, validation, tracking, and preparing submission package.

In addition, a biostatistician plays an important role by reviewing the statistical methodologies required for new analyses and providing guidance on appropriate statistical procedures for any additional analyses that may be necessary. Furthermore, a regulatory affairs representative ensures that the response aligns with regulatory expectations and offers insights into past regulatory interactions and relevant guidance documents. If applicable, a clinical and medical team contributes to the process by providing input on the clinical relevance and interpretation of the data.

When considering resource allocation, it is important to distribute the workload effectively, assigning tasks based on each team member's expertise and availability to prevent any individual from becoming overburdened. Additionally, having backup programmers available is advisable in case resource constraints arise. Finally, establishing a communication plan with regular check-ins will enable the team to monitor progress, address issues proactively, and ensure a smooth workflow throughout the IR response process.

DEFINING THE PROJECT TIMELINE

Developing a structured timeline ensures that all tasks are completed within the deadline. The timeline should incorporate all stages of the IR response process, including programming, validation, review, and submission. Key phases in timeline planning are described below:

Phase	Tasks Included
IR Review and Clarification	Understanding requests, clarifying ambiguities, discussing with biostatistician, clinical and regulatory affairs team
Data Extraction and Preparation	Identifying datasets, verifying data integrity, extracting required information
Statistical Programming and Analysis	Writing new programs, modifying existing scripts, generating tables/listings/figures
Validation and Quality Control	Double programming, cross-checking outputs, performing automated validation checks
Internal Review and Documentation	Reviewing results with biostatisticians, updating documentation, preparing submission files
Regulatory Submission Preparation	Finalizing outputs, formatting per regulatory requirements, and submitting through proper channels

Table 1. Key Phases and Tasks in Timeline Planning

When planning timelines for an Information Response (IR), several important factors must be considered. First, the urgency of the incident affects the timeline. High-priority incidents often require a quick response and more resources to handle them quickly. Second, the complexity of the analysis matters. New or unexpected analyses usually take more time than simple data checks. Lastly, it is important to keep regulatory deadlines in mind. Make sure there is enough time for a thorough internal review and validation before submitting the final dataset(s) or output(s).

MANAGING RISKS AND CONTINGENCY PLANNING

Despite careful planning, unforeseen challenges can arise. Identifying potential risks early and developing contingency plans ensures smoother execution.

Risk	Impact	Mitigation Strategy
Ambiguous IR Request	Delays due to misinterpretation	Seek clarification from regulatory and biostatistics teams immediately

Risk	Impact	Mitigation Strategy
Data Quality Issues	Missing or inconsistent data requiring re-extraction	Conduct early data checks and liaise with data management
Resource Unavailability	The programmer or statistician is unavailable due to other priorities	Assign backup personnel and maintain clear documentation for seamless handover
Validation Failures	Errors in analysis requiring rework	Incorporate sufficient validation time and peer review
Last-Minute Changes from the Regulatory/Clinical Team	Redoing analyses, leading to a time crunch	Maintain flexible programming approaches to allow quick modifications

Table 2. Common Risks, Impact, and Mitigation Strategies

MONITORING PROGRESS AND ADJUSTING TIMELINES

Tracking the progress of IR responses is essential to ensuring that tasks remain on schedule and that any potential delays are addressed promptly. Effective methods for monitoring progress include assigning tasks and tracking their completion using project management tools such as MS Project.

In addition to using project management tools, holding daily or weekly progress meetings with the team can facilitate discussions on status updates and any blockers encountered. Maintaining task checklists is also important for accountability, providing a clear view of completed and pending tasks.

If unexpected delays do occur, it is crucial to communicate with regulatory affairs as early as possible to discuss possible deadline extensions. Furthermore, dynamically reallocating resources to high-priority tasks can help ensure timely submission and minimize disruptions.

PLANNING VALIDATION ACTIVITIES

Validation is critical to ensuring the accuracy and consistency of Information Request (IRs) response. Statistical programmers must implement a robust validation plan to ensure accuracy by eliminating programming errors, data inconsistencies, and statistical miscalculations and to confirm its alignment with regulatory requests. A well-structured validation process minimizes the risk of discrepancies, enhances the credibility of submitted data, and facilitates a smooth regulatory review. Furthermore, adherence to CDISC standards, including SDTM and ADaM, guarantees compliance with regulatory guidelines.

Failure to thoroughly validate IR responses may result in regulatory rejections, requests for additional clarifications, or potential delays in the drug approval process.

VALIDATION PLAN

Validation methods should be tailored to the complexity and nature of the IR. The following validation approaches are commonly used:

- **Double Programming:** This approach ensures that the results are independently verified, reducing the risk of errors in critical analyses. Double programming systematically compares the original and validation results for discrepancies. Any mismatches identified during this process are thoroughly investigated and resolved to maintain data integrity. By implementing this method, statistical programmers can enhance the reliability of their outputs and ensure consistency across analyses.
- **Independent Programming:** In this approach, a separate programmer or biostatistician independently reproduces statistical analyses to validate the results generated by the development programmer. Independent programming by biostatisticians is essential for efficacy analyses, such as primary endpoints, inferential statistical tests, and models. They confirm that appropriate statistical techniques, models, and assumptions have been applied correctly per the study protocol and statistical analysis plan (SAP).

- **Peer Review / Code Review:** A second programmer reviews the original code line-by-line and checks the logic against the requirements in this approach. They may also review output for consistency with expectations. While less resource-intensive than double programming, code review can catch programming mistakes, ensure adherence to standards, and ensure the output matches the mock shells or SAP.
- **Log File Review:** Reviewing programming log files is an important step in ensuring the accuracy and integrity of deliverables. Programmers should look for errors, warnings, and note messages, as these can lead to incorrect analysis results. To maintain data quality and regulatory compliance, programmers must resolve all identified issues before delivering the final outputs.

QUALITY CONTROL (QC) DOCUMENTATION

Thorough documentation of all validation activities is important for establishing a clear audit trail. Regulatory agencies often require evidence of validation processes, making proper documentation essential. This practice ensures compliance and supports transparency and accountability in validation efforts.

Document	Purpose	Key Information Included
Validation Plan	Defines scope, methods, and timelines for validation.	Type of validation (double programming, independent programming, peer review/code review, etc.), assigned personnel.
Programming Specifications	Details of how the datasets and outputs were generated.	Dataset derivation steps, algorithms, and statistical methods.
QC Checklist	Ensures all validation steps are completed.	Checklist for dataset integrity, output verification, and log file review.
Validation Report	Summarizes findings from validation activities.	Any issues identified and their resolutions.

Table 3. Validation Documentation Components

HANDLING VALIDATION FAILURES

Validation failures in statistical programming for clinical trials can arise due to various factors, often related to data handling, programming logic, or methodological inconsistencies. Identifying the root cause of these failures is crucial for ensuring data integrity and compliance with regulatory standards. Below are some common root causes:

- **Data Issues**
    - **Missing or Incomplete Data:** Incomplete datasets, missing values, or unhandled NULL values can cause discrepancies in validation.
    - **Incorrect Data Mapping:** Misalignment between source data (e.g., SDTM) and analysis datasets (e.g., ADaM) may result in validation errors.
    - **Data Transformation Errors:** Issues in derived variables, such as incorrect calculations or unintended modifications, can lead to inconsistencies.
- **Programming Errors**
    - **Logic Errors:** Incorrect implementation of programming logic, such as wrong conditional statements, can lead to mismatched results.
    - **Syntax Errors:** Improper coding syntax or incorrect function usage may cause execution failures or inaccurate outputs.
    - **Code Version Mismatch:** Running different versions of code or using outdated scripts may lead to unexpected results.

- **Validation Methodology Issues**
    - **Incorrect Comparison Criteria:** Differences in validation methods, such as comparing datasets with mismatched keys or incorrect rounding rules, can cause failures.
    - **Inconsistent Statistical Methods:** Differences in statistical modeling, parameter selection, or software versions between the original and validation programs can lead to discrepancies.
- **Regulatory and Compliance Issues**
    - **Non-Adherence to Standards:** Deviations from CDISC standards (SDTM, ADaM) or regulatory guidelines may cause validation failures.
    - **Lack of Documentation:** Poor documentation of data derivations, transformation rules, or validation steps can make it difficult to identify the cause of discrepancies.
    - **Inconsistent Metadata Handling:** Differences in variable labels, formats, or controlled terminology between datasets may lead to validation mismatches.

To diagnose validation failures effectively, the following steps should be taken:

- **Review Log Files:** Identify errors, warnings, and notes that may provide clues about the issue.
- **Compare Input and Output Data:** Check for inconsistencies in datasets, formats, and transformations.
- **Examine Code Logic:** Debug scripts to verify whether calculations and conditions are implemented correctly.
- **Check Validation Methodology:** Ensure that the validation approach follows best practices and aligns with the original analysis.
- **Consult Documentation:** Review programming specifications, SAP, and CDISC guidelines to confirm compliance.
- **Communicate with Team Members:** Collaborate with statisticians, data managers, and other programmers to clarify discrepancies.

By systematically investigating these root causes, validation failures can be effectively resolved, ensuring high-quality and reliable clinical trial data submissions.

TRACKING AND SUBMISSION

From a statistical programmer's perspective, information requests (IRs) tracking involves accurate monitoring, ensuring that datasets and outputs are accurately generated, validated, and submitted in the required format. A well-structured tracking system enhances efficiency, reduces the risk of missed deadlines, and ensures seamless communication among cross-functional teams. The following section provides a comprehensive framework for tracking and submitting IRs to regulatory agencies.

IMPORTANCE OF TRACKING INFORMATION REQUESTS

Tracking IRs ensures that all regulatory agency requests are recorded, assigned, monitored, and completed on time. Since IRs often have strict deadlines (e.g., a 14-day turnaround for certain FDA requests), failing to track them properly can lead to serious consequences.

One major consequence of poor tracking is regulatory delays. Incomplete or late responses can prolong the review cycle and delay the drug approval process. Additionally, a lack of a structured tracking system increases the risk of data inconsistencies, where outdated or incorrect datasets may be submitted due to oversight. Effective tracking helps prevent miscommunication among regulatory and medical writing teams, biostatisticians, and programmers, ensuring clear ownership of each IR and avoiding duplication or missed responses. Furthermore, regulatory agencies expect sponsors to maintain control over their interactions, and inadequate tracking could lead to compliance issues.

HOW TO TRACK INFORMATION REQUESTS

Implementing a centralized tracking system or study-level tracking sheet is a best practice that ensures IRs are managed systematically and efficiently. The following table represents the key components of an IR tracking sheet.

Requesting Agency	Name of the requesting agency (e.g., FDA, EMA, MHRA, PMDA)
IR Number/ID	A unique identifier is assigned to each regulatory request
Question Number	Question number IR for which the response is being prepared
Request Date	Date of IR request
Submission Due Date	Date of submission due to the agency or to the regulatory/medical writing team
Dataset/TLF Name	Name dataset/TLFs being modified or newly created
Objective/Analysis of the Request	Describe the objective and type of analysis (e.g., PFS analysis by age)
Specification Location	Provide a link for the dataset or TLFs specification document
Expected Completion Date	Expected completion date, including double programming and STAT review
Statistician Name	Name of the study lead statistician
Developer Name	Name of the study lead or developer working on the request
Validator Name	Name of the programmer performing double-programming or code review
Data Cutoff Date	It helps to identify which data to use to draft the IR response
Folder Location	Folder location where all the responses are prepared for submission
Output File Location	Location of the output files (e.g., SDTM/ADaM datasets, TLFs)
Program Location	Location of developer program used to create response analysis
Validation Location	Location of validation folder where double-programming is performed
Development/Validation Status	Record the status of the development/validation activities
Completion Date	Completion date of the programming, including validation activities

Table 4. Key Components of Information Requests (IRs) Tracking Sheet

Real-time updates are crucial for maintaining visibility and keeping all stakeholders informed about the status of each IR. Regardless of the tool used, ensuring timely data entry and progress tracking enhances efficiency and minimizes bottlenecks.

SUBMISSION OF IR RESPONSES

Submitting Information Requests (IRs) response is the final step in the regulatory review process. It involves careful preparation, adherence to submission guidelines, and post-submission monitoring. Ensuring that IR responses are formatted correctly and submitted through the appropriate channels minimizes the risk of delays and facilitates a smooth regulatory review process. From a programmer's perspective, a well-structured submission package must include all necessary components in the required format. The key elements are:

- **Datasets:** Submission-ready SDTM/ADaM datasets in XPT format, validated and compliant with regulatory standards to ensure data integrity.
- **Define.xml and Reviewer's Guide:** Metadata documentation provides traceability of datasets and ensures transparency for regulatory reviewers.

- **Analysis Outputs (TLFs):** It must be formatted per agency guidelines to support statistical and clinical conclusions.
- **eCTD Format Compliance:** Ensuring all submission files adhere to electronic Common Technical Document (eCTD) specifications for regulatory compatibility.

Responses to Information Requests (IRs) must be submitted through the designated electronic submission portals specified by the relevant regulatory agency. It is crucial to ensure that submissions comply with the specific guidelines and formats required by each agency to facilitate timely review and processing. Following submission, it is essential to maintain oversight and be prepared for additional regulatory requests or follow-up questions. Key post-submission activities include:

- **Confirm Receipt:** Verify that the regulatory agency has received the submission and that no transmission issues occurred.
- **Monitor the Tracking System:** Keep the IR tracking system updated for any follow-up questions or additional requests from the agency.
- **Maintain a Document Repository:** Store all submitted documents in a centralized repository to ensure easy access for future audits, compliance checks, or references.

By following these best practices, sponsors can ensure timely and compliant IR submissions, facilitating a smoother regulatory review process and minimizing the risk of delays in drug approval.

CONCLUSION

Effectively handling Information Requests (IRs) from regulatory agencies requires a structured approach to ensure accuracy, compliance, and efficiency. Statistical programmers play a key role in gathering data, performing validation, and tracking responses to meet regulatory deadlines. A robust validation process, including double programming and independent reviews, ensures data integrity and compliance with CDISC standards. Implementing a centralized IR tracking system minimizes delays and enhances coordination across teams. Clear documentation, collaboration with biostatisticians and regulatory affairs, and adherence to submission guidelines streamline the process. By following best practices, statistical programmers can improve the quality of IR responses, facilitating timely regulatory reviews and drug approvals.

REFERENCES AND RECOMMENDED READING

- U.S. Food and Drug Administration (FDA). *"FDA Guidance for Industry: Providing Regulatory Submissions in Electronic Format -Standardized Study Data"* Retrieved from https://www.fda.gov/industry/fda-data-standards-advisory-board/study-data-standards-resources
- U.S. Food and Drug Administration (FDA). "Study Data Technical Conformance Guide" Retrieved from https://www.fda.gov/regulatory-information/search-fda-guidance-documents/study-data-technical-conformance-guide-technical-specifications-document
- International Council for Harmonisation (ICH). *"ICH E6(R2) Good Clinical Practice (GCP) Guidelines"* Retrieved from https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf
- International Council for Harmonisation (ICH). *"ICH E9 Statistical Principles for Clinical Trials"* Retrieved from https://database.ich.org/sites/default/files/E9_Guideline.pdf
- Pinnacle 21. *"Using Pinnacle 21 Enterprise for define.xml Creation"* Retrieved from https://www.lexjansen.com/pharmasug/2019/PO/PharmaSUG-2019-PO-066.pdf

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