

Paper SA04Interactions and Communications with Regulatory Agencies during Submission Process

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Abstract

Effective interactions and communications with regulatory agencies are crucial elements throughout the regulatory submission and approval process, which involves meaningful engagements with the agencies to facilitate regulatory review of pharmaceutical products' safety, efficacy, and quality. This paper discusses the importance of establishing a collaborative relationship and provides an overview of key attributes in navigating the regulatory landscape, such as FDA, EMEA, PMDA, or NMPA, in relation to the submission process. Specifically, it describes the significance of establishing effective and transparent communication channels with regulatory agencies, understanding local regulatory requirements and processes, considering cultural sensitivities, timely responses to queries, proactive engagement to address regulatory concerns, and compliance with regulatory requirements. The paper also briefly describes initiatives involving development of innovative cloud-based platforms to support real-time sponsor-regulator interactions, collaborations, as well as data and document exchanges that enable rapid review, feedback, and approval.

Introduction

Interacting and communicating effectively with regulatory agencies is crucial during the drug submission and approval process. Through interactions, pharmaceutical companies can gain insights into regulatory requirements and expectations, which helps to ensure compliance throughout the drug development process. The timely interactions with regulatory agencies to discuss study design, endpoint selection, data analysis, and data interpretation help to ensure that the drug development program meets regulatory expectations and scientific standards, leading to more robust and credible data submissions. Regular communications with regulatory agencies not only potentially accelerate the approval timelines but can also help sponsor companies in proactively addressing any issues before they become major problems.

Role of Regulatory Agencies

Regulatory agencies play an important role in safeguarding public health by ensuring that the drugs are safe, effective, and of high quality before they are made available to patients. In general, the regulatory agencies

are involved in reviewing applications, oversight of clinical trials, risk assessment, regulation of labeling and packaging, post-market surveillance, and enforcement of compliance with regulations and guidelines.

Importance of Interaction and Communication

Regulatory agencies have strict guidelines and regulations that drugs must adhere to for approval. Understanding the requirements and expectations of regulatory agencies helps companies tailor their development plans. Regulatory communications, including pre-defined agency meetings such as pre-NDA and AOM, help ensure that the drug development process meets the regulatory guidelines and requirements, minimizing the risk of delays or rejections. As regulatory agencies provide valuable feedback on clinical trial designs, data requirements, safety considerations and so on, utilizing this support can address any concerns or issues early in the process and enhance the quality of the drug development program and increase the likelihood of approval. Early and ongoing engagement allows for timely feedback and identification of regulatory risks and uncertainties. Establishing open lines of communication with regulatory agencies helps in building relationships and credibility, which can lead to smoother interactions and potentially faster, collaborative review processes.

Pre-Submission Interaction

Pre-submission interactions are highly important in the context of project management or in preparing for any official submission. This is a key opportunity to discuss what to include in the data and how it should be organized. By discussing the submission with regulators beforehand, the sponsors can reduce the chances of making errors and omissions that could lead to delays or rejections. These interactions provide an opportunity for the team to review and discuss the submission requirements including unique aspects of data collection and/or analysis, clarify any uncertainties, finalize details and ensure that all necessary elements are in place before the actual submission. These interactions help to facilitate constructive feedback and review, timeline discussions, and allow identification and discussion of potential risks or challenges associated with the submission. This proactive approach helps in developing mitigation strategies to address these issues. Any pre-submission meetings with regulatory agencies facilitate constructive feedback and review among team members. Peer review and feedback sessions can enhance the quality of the submission by incorporating diverse perspectives and insights.

Documentation Based Interaction

The guidance documents, technical conformance guides, and presentations published by the regulatory agencies, and the study documents, including metadata, submitted by the sponsor companies constitute an ongoing form of interaction between both parties. The regulatory guidance documents provide the agency's understanding, expectations and requirements on different processes and deliverables. These documents are used by the sponsor companies as instructions in preparation and submission of the

submission packages. On the other hand, the sponsor companies communicate with the regulatory reviewers by providing the required or specific information to facilitate the review in the study documents included in the submission package. Some of the examples of such documents are study protocol, statistical analysis plan, data handling rules, annotated case report forms, define.xml, and reviewer's guides.

Communication During Review Process

Communicating effectively with regulatory agencies during the review process is important for several reasons. Communication allows sponsors to seek clarification on regulatory requirements and guidelines. Agencies can provide guidance on submitting information in response to IRs, understanding specific requests or feedback, and addressing any uncertainties. Engaging with regulatory agencies helps in staying informed about the status of the submission. This can include updates on the review timeline, potential issues or concerns raised during the review, and any additional information needed. If regulatory agencies have questions or concerns about the submission, open communication channels allow sponsors to address these issues promptly. This can help prevent delays in the review process and facilitate a smoother path to approval. Building a positive and professional relationship with regulatory agencies can be beneficial for future submissions. Establishing trust and rapport through communication may lead to more efficient reviews and a better understanding of the application by the agency.

Addressing questions and concerns raised by regulatory agencies is a crucial aspect of compliance for any organization. Here are some strategies to effectively handle such situations:

- Take regulatory agency inquiries seriously and respond promptly to demonstrate commitment to compliance.
- Conduct a thorough internal investigation to understand the issue fully before responding to the regulatory agency.
- Provide clear and concise explanations to address the concerns raised by the regulatory agency. Use plain language to ensure clarity.
- Cooperate with the regulatory agency during the investigation process and provide all necessary information and documents as requested.
- Review internal compliance policies and procedures to identify any gaps that may have led to the concerns raised by the regulatory agency.
- Take appropriate remedial action to address any issues identified by the regulatory agency and prevent similar occurrences in the future.
- Keep detailed records of all communications and actions taken in response to the regulatory agency's inquiries to demonstrate compliance efforts.

Preparing and submitting responses to regulatory queries is important for compliance and maintaining good relationships with regulatory authorities. Here are some tips to help navigate this process effectively:

- Carefully read and analyze the regulatory query to fully comprehend the requirements and expectations of the regulatory authority.

- Collect all relevant documents, data, and information needed to respond to the query for completeness and accuracy, and to provide as supporting evidence
- Create a structured plan outlining how each aspect of the query will be addressed.
- Respond to regulatory queries within the stipulated timeframe to demonstrate commitment to compliance and cooperation.
- Present the response in a clear and concise manner, focusing on addressing each specific point raised in the query.
- If there are any doubts or need further clarification on the regulatory query, do not hesitate to seek clarification from the regulatory authority.
- Before submitting the response, thoroughly review and validate the content to ensure accuracy, completeness, and compliance with regulatory requirements.
- Be honest and transparent in responses to regulatory queries.
- Maintain a record of all communication and documentation related to the regulatory query and response process for future reference and audit trail purposes.

Providing timely and thorough responses during the drug approval process is critically important to ensure a smooth review process. Here are some reasons why it is essential:

- Timely responses are necessary to comply with regulatory requirements and timelines set by health authorities.
- Thorough responses provide the necessary information for regulatory authorities to assess the safety and efficacy of the drug.
- Timely and comprehensive responses demonstrate the commitment of the drug sponsor to provide accurate and high-quality data.
- Delays in the approval process prevent patients from accessing potentially life-saving medications.
- A smooth and efficient approval process can give a company a competitive advantage in the market by enabling earlier market entry and commercialization of the drug.

Cloud-based Interactive Interactions- Examples

With the advances in overall technology and, specifically cloud-based technologies, both regulatory agencies as well as industry are considering initiatives to have more efficient interactive interactions and data exchanges between the regulatory agencies and sponsors, and within the agencies and the sponsors. This paper briefly talks about two such initiatives: FDA's PRISM Project^[1] and Accumulus Platform^[2]. The FDA's PRISM (PrecisionFDA Regulatory Information Service Module) Project is a proof-of concept and research collaboration between FDA and industry companies to explore utilization of FDA's production regulatory cloud platform, PrecisionFDA, to streamline, improve, and enable a variety of applicant-regulator interactions, including submission, review, and ease of communications for human drug and biologics applications to FDA. The Accumulus Platform is a modern solution, cloud-based data exchange platform to improve collaboration and real-time information exchange. between life sciences organizations and regulatory authorities.

Conclusion

In conclusion, interactions and communications with regulatory agencies are essential for drug submission and approval. By engaging early and proactively with regulatory bodies, companies can enhance regulatory compliance, expedite approval timelines, mitigate risks, foster scientific dialogue, and ultimately drive towards improved market access and commercial success for their drug products.

References

[1] An Introduction to PRISM (PrecisionFDA Regulatory Information Service Module) by Ginny Hussong at PHUSE/FDA Computational Science Symposium – June 3, 2024, Silver Spring, MD

[2] accumulus.org

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