



HEALTH AUTHORITY INTERACTIONS AND COMMUNICATIONS

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Submission and Agencies



Presentation Topics

- Key roles and responsibilities of regulatory agencies in approving new drugs
- Importance of Interaction and Communication
- Interactions *via* Documentation
- Pre-Submission Interaction
- Communication During Review Process
- Responding to Regulatory Queries
- Cloud-based Interactive Interactions- Examples

Regulatory Agencies

Key roles and responsibilities of regulatory agencies in drug approval include:-

- Reviewing Applications
- Clinical Trials Oversight
- Risk Assessment
- Regulation of Labeling and Packaging
- Post-market Surveillance
- Enforcement

Regulatory Agencies

List of key regulatory agencies involved in drug approval process

- Food and Drug Administration (FDA) - United States
- Pharmaceuticals and Medical Devices Agency (PMDA) – Japan
- National Medical Products Administration (NMPA) - China
- European Medicines Agency (EMA) - European Union
- Medicines and Healthcare products Regulatory Agency (MHRA) - United Kingdom
- Health Canada (HC) - Canada
- Therapeutic Goods Administration (TGA) - Australia
- Central Drugs Standard Control Organization (CDSCO) - India
- Swissmedic - Switzerland
- Health Sciences Authority (HSA) - Singapore

Overview of Drug Development Process

- Preclinical Research:
 - This phase involves extensive laboratory and animal studies to test the safety and efficacy of the drug.
- Investigational New Drug (IND) Application:
 - Once preclinical research is completed, the sponsor (usually a pharmaceutical company) submits an IND application to the regulatory authorities (such as the FDA in the US) to begin clinical trials in humans.
- Clinical Trials:
 - This phase involves testing the drug on human subjects to determine its safety and efficacy. Clinical trials are conducted in multiple phases, with each phase providing more data on the drug's effectiveness and safety.
- New Drug Application (NDA) Submission:
 - After successful completion of clinical trials, the sponsor submits an NDA to the regulatory authorities seeking approval to market the drug.
- Regulatory Review:
 - Regulatory authorities review the NDA to ensure that the drug is safe and effective for its intended use. This review process can take several months to years, depending on the complexity of the drug and the data submitted.
- Approval:
 - If the regulatory authorities determine that the drug is safe and effective, they will approve the drug for market. This approval allows the sponsor to begin marketing the drug to healthcare professionals and the public.
- Post-Marketing Surveillance:
 - After approval, the drug is monitored for any unexpected side effects or safety concerns through post-marketing surveillance. This helps to ensure the ongoing safety of the drug for patients.

Importance of Interaction and Communication

Effective interactions and communications with regulatory agencies throughout the regulatory submission and approval process facilitate:-

- Regulatory compliance
- Application approval
- Risk mitigation
- Scientific dialogue
- Market access

Importance of Interaction and Communication

- Regulatory guidance:
 - Understanding the requirements and expectations of regulatory agencies help the sponsors build robust protocols, development plans, and post-submission strategies..
- Compliance with regulations:
 - Regular communications help ensure that the drug development process follows the rules, minimizing the risk of delays or rejections.
- Risk identification and mitigation:
 - This proactive approach can help avoid costly delays and improve the chances of approval.
- Transparency and trust:
 - Open communication fosters a positive relationship and can lead to a more collaborative review process.

Importance of Interaction and Communication

Importance of having early engagement with regulatory agencies throughout the process

- Understanding requirements:
 - This can help in designing the development process to meet those requirements from the beginning, reducing the risk of delays or rejections later on.
- Timely feedback:
 - This feedback can help to address potential issues or concerns early on, leading to more efficient product development.
- Building relationships:
 - This can lead to smoother interactions and potentially faster reviews and approvals when it comes time to submit your product for regulatory approval.
- Risk mitigation:
 - By addressing these issues proactively, risks can be mitigated and avoiding costly delays in the future.

Pre-Submission Interaction

- Clarity on requirements:
 - Pre-submission interactions help to ensure clarity about the requirements of the submission. This clarity is crucial to avoid overlooking important details and to meet all the submission criteria. These interactions presents opportunity for the sponsor to discuss any unique aspects of the data collection and/or analysis, as well as any special requirements for data submission. This is a key opportunity to discuss what to include in the data and how it should be organized.
- Coordination and consistency:
 - These interactions enable coordination of efforts and ensure consistency in the submission. It allows for different team members to align their work and contributions, leading to a cohesive final submission.
- Risk identification:
 - Pre-submission interactions provide a platform to identify and discuss potential risks or challenges associated with the submission. This proactive approach helps in developing mitigation strategies to address these issues.
- Feedback and review:
 - These interactions facilitate constructive feedback and review. Peer review and feedback sessions can enhance the quality of the submission by incorporating diverse perspectives and insights.
- Timelines and deadlines:
 - Discussing timelines and deadlines during pre-submission interactions ensures both sides are aware of crucial dates and can align their work accordingly. This helps in meeting submission deadlines and managing time effectively.
- Quality assurance:
 - By reviewing the submission components during pre-submission interactions, the sponsors can ensure the quality of the submission is up to the expected standards. This ensures that the final submission is of high quality and reflects the team's collective effort.

Pre-Submission Interaction

How these interactions can help clarify regulatory expectations and requirements

- Clear guidance:
 - These interactions provide an opportunity to seek clarification on any regulatory requirements that may be unclear.
- Reduce errors:
 - Beforehand discussion of the submission with regulators can reduce the chances of making errors or omissions that could lead to delays or rejection.
- Address issues early:
 - If there are any potential concerns or issues with the submission, the pre-submission interactions allow to address them early on and make corrections before submitting the application.
- Build relationships:
 - Building a relationship with regulatory authorities through these interactions can be beneficial in fostering communication and understanding between both parties.
- Improve submission quality:
 - By getting feedback and guidance from regulators during these interactions, the overall quality of the submission can be improved.

Documentation Based Interaction

- From Regulatory agencies' perspective:
 - Guidance documents
 - Technical Conformance Guides (TCGs)
 - Presentations
 - Data Standards Catalog
 - Validation rules
- From Industry perspective:
 - Study protocol
 - Statistical Analysis Plan (SAP)
 - Data handling/integrity rules
 - Annotated Case Report Form (acrf.pdf)
 - Data Reviewer's Guides
 - define.xml
 - Analysis Results Metadata (ARM)
 - Trial design domains

Communication During Review Process

Importance of communication during the review process

- Clarification and guidance:
 - Regular communications allow to seek clarification on regulatory requirements and guidelines. Agencies can provide guidance on the submission process, help understand specific requests or feedback, and address any uncertainties.
- Timely updates:
 - Engaging with regulatory agencies helps to stay informed about the status of the submission. This can include updates on the review timelines, potential issues or concerns raised during the review, and any additional information needed.
- Issue resolution:
 - If regulatory agencies have questions or concerns about the submission, open communication channels allow to address these issues promptly. This can help prevent delays in the review process and facilitate a smoother path to approval.
- Relationship building:
 - 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 product by the agency.

Communication During Review Process

Strategies for effectively addressing questions and concerns raised by regulatory agencies

- Prompt response: Take regulatory agency inquiries seriously and respond promptly to demonstrate commitment to compliance.
- Thorough investigation: Conduct a thorough internal investigation to understand the issue fully before responding to the regulatory agency.
- Clear communication: Provide clear and concise explanations to address the concerns raised by the regulatory agency. Use plain language to ensure clarity.
- Cooperation: Cooperate with the regulatory agency during the investigation process and provide all necessary information and documents as requested.
- Compliance review: Review internal compliance policies and procedures to identify any gaps that may have led to the concerns raised by the regulatory agency.
- Remedial action: Take appropriate remedial action to address any issues identified by the regulatory agency and prevent similar occurrences in the future.
- Documentation: Keep detailed records of all communications and actions taken in response to the regulatory agency's inquiries to demonstrate compliance efforts.
- Legal guidance: Seek legal advice if needed to ensure that the responses are in compliance with relevant laws and regulations.

Responding to Regulatory Queries

Tips for preparing and submitting responses to regulatory queries

- Understand the query:
 - Carefully read and analyze the regulatory query to fully comprehend the requirements and expectations of the regulatory authority
- Gather relevant information:
 - Collect all relevant documents, data, and information needed to respond to the query. Ensure that the response is supported by accurate and up-to-date information.
- Develop a response plan:
 - Create a structured plan outlining how each aspect of the query will be addressed. Assign responsibilities to individuals or teams involved in preparing the response to ensure a coordinated effort.
- Team effort:
 - Regulatory query may also need input from other groups, like clinical, safety, pharmacometrics, and regulatory, depending on the nature of the query. Preparing a response is a team effort.
- Be timely:
 - Respond to regulatory queries within the stipulated timeframe to demonstrate commitment to compliance and cooperation. If additional time is needed, communicate this proactively with the regulatory authority.
- Be concise and clear:
 - Present the response in a clear and concise manner, focusing on addressing each specific point raised in the query. Avoid unnecessary technical jargon or vague language that could lead to misunderstandings.

Responding to Regulatory Queries

- Provide supporting evidence:
 - Back up the response with relevant documentation and evidence to substantiate the claims and demonstrate compliance with applicable regulations.
- Seek clarification, if needed:
 - If there are any doubts or need further clarification on the regulatory query, do not hesitate to seek clarification from the regulatory authority. It is better to ask for clarification upfront than to provide an inaccurate or incomplete response.
- Review and validate:
 - Before submitting the response, thoroughly review and validate the content to ensure accuracy, completeness, and compliance with regulatory requirements. Consider obtaining a second opinion from a subject matter expert, if necessary.
- Maintain transparency:
 - Be honest and transparent in the responses to regulatory queries. Disclose any relevant information, even if it may reflect negatively on the organization, to establish trust and credibility with the regulatory authority.
- Keep a record:
 - Maintain a record of all communications and documentation related to the regulatory query and response process for future reference and audit trail purposes.

Responding to Regulatory Queries

Providing timely and thorough responses ensures a smooth review process

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

Cloud-based Interactive Interactions- Examples

- **FDA's PRISM (PrecisionFDA Regulatory Information Service Module) Project:**
 - 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.
- **PrecisionFDA Spaces:**
 - Building blocks to enable applicant-regulator interactions
 - Dedicated, secure, private spaces for applicants and regulators
 - Interactive review space shared by both applicants and regulators
 - Users can work in only those spaces which are available to them
 - Users can copy files to/from the assigned private and shared spaces
- Shared tools available to both applicants and regulators to facilitate interaction
- Two-way flow of information and communication between the FDA and sponsor in shared space

Cloud-based Interactive Interactions- Examples

- **Accumulus synergy:**
 - A nonprofit technology organization – backed by 12 life-sciences sponsor companies – is developing a cloud-based data exchange platform to improve collaboration between life sciences organizations and regulatory authorities.
 - Fourteen participating national regulatory authorities worldwide
 - The Accumulus Platform is a modern solution for regulatory interactions; for secure real-time information exchange among industry and regulatory stakeholders.
- **Key Features of the Accumulus Platform:**
 - Improves collaboration for users of all regulatory maturity levels through an easily accessible platform
 - Offers full document-based upload with content display for a centralized view of information
 - Reduces administration burden, strengthens operational efficiency, and drive visibility
 - Provides real-time data exchange that enables rapid review and feedback

Thank you!