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Regulatory Compliance for Drugs and Biologics

ENET Panel DIscussion

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Different Drug/Biologics Pathways

IND: a drug developed by a pharmaceutical or biotech company that is ready for clinical trials on humans

NDA: an application to permit the sale and marketing of a new drug in the United States. A traditional NDA consists of data and information about the drug as gained from both nonclinical and clinical studies, as well as a summary of formulation development and manufacturing processes, and proposed labeling information to be included in the drug's packaging.

BLAs relate to biological products while NDAs generally pertain to traditional small molecule drugs.

Where do you file?

There are two Centers within the FDA that are responsible for the review and approval of drugs and general regulatory oversight:

- the Center for Drug Evaluation and Research (CDER)
- the Center for Biologics Evaluation and Research (CBER).
- While all conventional drug products (i.e., small molecules) are regulated by CDER, biological products can be regulated by either CDER or CBER

- The majority of BLA submissions are assigned to CBER; however, BLAs for certain biological product categories are reviewed by CDER instead
    - monoclonal antibodies for *in vivo* use
    - most proteins for therapeutic use (e.g., cytokines, enzymes
    - other novel proteins except those assigned to CBER, such as vaccines and blood products), immunomodulators, and growth factors. Regardless of the category, NDAs for all drug products fall under the jurisdiction of CDER.

Appropriate for drug products that are the same as approved products

Hatch Waxman 1984 led to a variety of Filing Options

Three drug pathways exist for NDAa

505(b)1: “vanilla” drug filing

505(b)2: A 505(b)(2) NDA contains full safety and effectiveness reports but allows at least some of the information required for NDA approval, such as safety and efficacy information on the active ingredient, to come from studies not conducted by or for the applicant. This can result in a much less expensive and much faster route to approval, compared with a traditional development path [such as 505(b)(1)], while creating new, differentiated products with tremendous commercial value

Generic: Same as an approved product (PD and PK)

Ideal 505(b)(2) candidates include:

- Drugs with new indications
- Drugs with changes in dosage form, strength, formulation, dosing regimen or route of administration
- New combination products/Drug-device combinations
- Prodrugs of an existing drug
- In some cases, drugs with new active ingredients
- Orphan drugs

Biological therapeutics, so-called biosimilars, are not suitable for approval under the 505(b)(2) pathway.

Drug Development and the FDA

Drug development

- Regulatory Filings
- FDA review and Approval Process
- Post Approval Submissions

FDA communication

- Direct (email, phone calls)
- Recalls
- Post approval submissions

Overview of Regulatory Compliance

- Provides assurance that all aspects of drug development are conducted in compliance with good practice regulation
- In a fully integrated pharmaceutical company (FIPCO) this includes review of many areas, including:
  - sales and marketing practices
  - drug pricing
  - privacy of patient or customer health information
  - clinical operations
  - post-marketing and drug safety reporting
  - quality control activities around manufacturing

Eliminates Risk

Goal is to Identify, mitigate and eliminate RIsk

- Enhances Investor and Customer Confidence
- **Saves money**
  - Expensive to conduct but cost of non-compliance is higher
- High quality products lead to safe products

There is no alternative to meeting regulatory compliance requirements

Managing CMOs

Virtual/Semi-virtual companies use CMOs to advance drug development.
This raises a unique set of issues as their operations are not under your control **but you are responsible for their activities for product quality, safety, efficacy and cGMP compliance**

- It is Important you have a robust CMO management system
  - Selection and qualification
  - CMO audits
  - Quality Agreements
  - Oversight of CMO operations
  - Review of key CMO records

Auditing and Outsourcing

- Auditors- what are you looking for in qualifications
- Using contractor support
- Internal auditing procedures and schedules
  - Key/critical audit area
  - Audit expectations
- Staff training

Management Oversight

- Quality policy
- Management review
- Escalation of issues to upper management
- Communication, decision making
- resourcing

And now for something completely different