The New Drug Approval Process

Margaret Kober, R.Ph., M.P.A.
Chief, Project Management Staff
Office of Regulatory Operations
Office of New Drugs
Center for Drug Evaluation and Research

Topics

- Pre-NDA activities
- Application types
- Application requirements & content
- Application review milestones
- Communications

Pre-NDA activities

Pre-IND meeting

Discussion with therapeutic area division (see https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/cder-offices-and-divisions to determine the appropriate division):

- Data requirements for IND application
- Data needed to support rationale for testing drug in humans
- Design of animal model studies (nonclinical pharmacology, toxicology) and drug activity studies
- Initial drug development plans
- Regulatory requirements for safety and efficacy demonstration

Well-designed and well-conducted foreign clinical trials need not be conducted under an IND if certain conditions are met (21 CFR 312.120 & 21 CFR 314.106). Examples include:

- FDA can inspect the clinical site and validate data
- data are applicable to the U.S. population and U.S. medical practice
- investigators are of recognized competence

Meetings are available throughout the research stages

User Fees must be paid before an application is submitted – small business waivers are available

NDA Types: 505(b)(1) vs 505(b)(2)

Refers to language in the Food, Drug, and Cosmetic Act

b1: own or have right of reference to all data

b2: rely on part on literature or the Agency's finding of safety and/or effectiveness for one or more listed drugs

NDA Types: Priority vs Standard

- Standard Review
  - Non- NME: 10-month clock
  - NME (under the Program): 12-month clock

- Priority Review
  - Non- NME: 6-month clock
  - NME (under the Program): 8-month clock

Priority Review

Criteria:

- treats a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness

OR

- proposes a labeling change pursuant to a report on a pediatric study (not all qualify)

OR

- has been designated as a qualified infectious disease product

OR

- submitted with a priority review voucher

Approval Types

- Full

  approved for use according to the agreed-upon labeling
- Tentative

  unresolved patent/exclusivity issues

  product can not be marketed
- Subpart H – accelerated approval

  Approval based on surrogate endpoint

  Confirmatory post-approval trial required

Application Requirements

- Correct application type
  - NDA vs BLA
  - NDA vs ANDA
- All required content
- eCTD format
- Firm is not in arrears for user fees

Application Contents

- All relevant content items and information
- Reports of all investigations of drug product sponsored by applicant and all other pertinent information
- Information may be incorporated by reference
  - Letter of Authorization (LOA)
- English translations

Application content

Module I: Regional Administrative Information

- Application form
- Debarment statement
- Patent information and Patent certification
- Claimed exclusivity
- Labeling

Application Content

- **Module II (Summary Overview):**
  - **Quality Overall Summary (data)**
  - **Clinical Overview (conclusions)**
  - **Clinical Summary**
  - **Nonclinical Overview**
  - **Nonclinical Summary**

Application Content

- **Module III: Quality**
- **Module IV: Nonclinical**
- **Module V: Clinical**
  - Medical – includes ISS + ISE
  - Clinical Pharmacology
  - Statistical
  - Clinical Microbiology

Review Milestones

- Submission
- Assembling a review team
- Filing
- Advisory Committee Meetings
- Action

Milestones

- Assembling a review team:
  - Clinical
  - Regulatory
  - Nonclinical pharmacology/toxicology
  - Chemistry (Quality)
  - Clinical pharmacology
  - Biostatistics
  - Consultants (device, botanical, ethics, controlled substance staff, patient labeling staff, pediatric experts)

Filing

- If refusing to file, FDA must communicate decision (and reasons) within 60 days of receipt
- Applicant may dispute
- Application can be filed over protest
    - No amendments
    - No meetings

Communications

Meetings

- Pre-submission
- Mid-Cycle (program applications)
- Late-Cycle (program applications)
- Labeling discussions

Communications

- Secure email – SecureEmail@fda.hhs.gov
- Regulatory Project Manager is the single point of contact
- Discuss preferences early on
- Review Issues will be communicated at day 74 if the application is filed
- Promptly respond to information requests

Advisory Committee Meetings

Purpose: To provide advice on technical and medical issues related to safety, effectiveness, testing, labeling, and the use of new drugs

Advisory Committee Meetings

Most often considered for:

- new drugs expected to have a major therapeutic impact, or major new uses of marketed drugs
- major safety concerns
- clinically meaningful difference vs. statistical meaningful difference
- surrogate markers; secondary endpoints