Center for Drug Evaluation and Research
Small Business and Industry Assistance (CDER SBIA) and New Drug Review

Renu Lal, Pharm.D.
CDER Small Business and Industry Assistance
Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
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Session Overview

- CDER SBIA Program
- Organizational Framework and Regulatory Authority
- New Drug Development Process
- Financial Incentives
**FDA Mission:** Promote and protect public health

**CDER Mission:** Promote and protect the health of Americans by assuring that prescription and over-the-counter drugs are safe and effective.

**CDER SBIA Mission:** Promote productive interaction with regulated domestic and international small pharmaceutical business and industry by providing timely and accurate information relating to development and regulation of human drug products.
CDER SBIA

- FDA recognizes that regulated small business and industry may encounter some difficulties in working through the complex regulatory process.

- Each regulatory Center has established a small business assistance office.

- Provide technical assistance and an efficient channel through which small business and industry can acquire information from the FDA.
CDER Small Business and Industry Assistance (CDER SBIA)

Search the CDER Small Business and Industry Assistance Section

(Formerly known as CDER Small Business Assistance)

The Information Source for Regulated Domestic and International Small Pharmaceutical Business and Industry

Small pharmaceutical business and industry are integral in bringing innovative medical products to the U.S. marketplace. The purpose of this website is to support CDER's Small Business and Industry Assistance (SBIA) Program's mission of promoting productive interaction with regulated domestic and international small pharmaceutical business and industry by providing timely and accurate information relating to development and regulation of human drug products.

Please take our short survey to help us improve our program and better serve you!

Drug Review Process

- Addresses for CDER Regulatory Submissions
- Generic Drug Review Process
- New Drug Development and Review Process
  Process for development of new drugs and therapeutic biologics, 505(b)(2). Meetings with FDA, Drug development costs, Statistics
- Over-the-Counter Drug Review Process
CDER SBIA

- **Phone**
  - 301-796-6707
  - 866-405-5367

- **Email:** [CDERSBIA@fda.hhs.gov](mailto:CDERSBIA@fda.hhs.gov)
- **Website:** [http://www.fda.gov/CDERSBIA](http://www.fda.gov/CDERSBIA)
FDA Organizational Framework

US Food and Drug Administration (FDA)

- Office of Regulatory Affairs (ORA)
- Center for Food Safety and Applied Nutrition (CFSAN)
- Center for Veterinary Medicine (CVM)
- National Center for Toxicological Research (NCTR)
- Center for Devices and Radiological Health (CDRH)
- Center for Tobacco Products (CTP)
- Center for Biologics Evaluation and Research (CBER)
- Center for Drug Evaluation and Research (CDER)
Scientific Review Staff

Reviewers specialize in

- Clinical (M.D.)
- Pharmacology/Toxicology (Ph.D.)
- Regulatory Project Management (R.N., Pharm.D.,)
- Chemistry (Ph.D.)
- Clinical Pharmacology/Biopharmaceutics (Ph.D., Pharm.D.)
- Statistics (Ph.D.)
- Microbiology (Ph.D.)
The Role of the Review Division

- Provide advice and guidance to regulated industry during drug development

- Signatory authority for regulatory decisions related to new (i.e., not generic) drugs
  - Work in conjunction with the other offices within CDER

- Establish policy and procedures governing the above
Where does our regulatory authority come from?

Code of Federal Regulations

- Written in response to laws passed by Congress
  - Represents how FDA interprets the Acts or laws which Congress passes

- Several Volumes
  - General and specific sections devoted to different FDA product areas (e.g., drugs, devices, and biologics)
What are Guidance Documents?

- Distinctly separate from the CFR
  - Represent the Agency’s current thinking on a particular subject
  - Provide flexibility as technology and drug development processes evolve
Regulatory Authority

- CDER regulates
  - Based on therapeutic health claim in the
    - application
    - label and packaging
    - advertising (for prescription drugs)
- CDER does not regulate
  - the practice of medicine
  - compounds that do not make a health claim
Is Your Product a Drug?

DRUG:

➢ Is your product or product idea intended to cure, treat, mitigate, diagnose, or prevent disease in humans, or is your product (other than food) intended to affect the structure or function of the human body? **Yes**

➢ Does your product achieve its primary intended purposes through chemical action and is your product metabolized by the human body? **Yes**
New Drug Development Process
Preclinical Research

- Discovery/Screening
- Synthesis and Purification
- Animal Testing
  - Evaluate drug’s toxic and pharmacologic effects

Determine whether the compound is safe for use in humans
Pre-Clinical R&D | Phase 1 | Phase 2 | Phase 3 | FDA Review | Phase 4

- Pre-IND Meeting
- EOP2 Meeting
- Pre-NDA/BLA Meeting
- AC Meeting
- Post-marketing Commitments
- Labeling & Risk Evaluation Meetings

SAFETY

Submit IND
Submit NDA/BLA Application

EFFICACY
Investigational New Drug Application (IND)

- Needed generally whenever studies in humans are conducted in the U.S. except:
  - Drug is lawfully marketed in the U.S. and investigation is not intended to support change in labeling or advertising and does not change the known risk/benefit profile (Exemptions 21 CFR 312.2(b))
  - Some bioavailability/bioequivalence studies (21 CFR 320.31(d))
  - Radioactive drugs for certain research purposes (21 CFR 361.1)

- Studies not conducted under an IND still require IRB approval and informed consent

- Guidance: INDs – Determining Whether Human Research Studies Can Be Conducted Without an IND
  - [http://tinyurl.com/INDGuidance](http://tinyurl.com/INDGuidance)
Pre-IND Consultation Program

- To foster early communications between sponsors and new drug review divisions in order to provide guidance on the data necessary to warrant IND submission

- Pre-IND Consultation List
  - [http://www.fda.gov/CDERSBIA](http://www.fda.gov/CDERSBIA)
  - New Drug Development and Review Process
  - IND Webpage
  - Pre-IND Consultation Program
Pre-IND Meeting

- Discussion with FDA staff prior to filing Investigational New Drug Application (IND)
- Opportunity to discuss:
  - Chemistry, Manufacturing, Controls (CMC) issues
  - Preclinical studies
  - Initial clinical protocol design
- Should have data and a development strategy
- Pre-set, well defined questions
- FDA offers suggestions, clarifies data requirements and study design
Does the IND meet Regulatory Requirements?

- 21 CFR 312.33
- Guidance for Industry
  - Content and Format of INDs
  - (Phase 1 and Phase 2/3)
Pre-Clinical R&D

Pre-IND Meeting

Phase 1

Phase 2

EOP2 Meeting

Phase 3

Pre-NDA/BLA Meeting

FDA Review

AC Meeting

Phase 4

Post-marketing Commitments

Submit IND

Submit NDA/BLA Application

SAFETY

EFFICACY

Labeling & Risk Evaluation Meetings
Clinical Studies

- **Phase I - First human subject studies**
  - Determine pharmacologic and metabolic activity, safety and maximum tolerated dosage in humans, side effects with increasing dose

- **Phase II**
  - Determine effectiveness for a particular indication, short-term side effects and risks, characterization of dose identification and dose response

- **Phase III – Large, controlled multicenter studies**
  - Gathers additional safety and efficacy information, addresses special issues/populations, provides basis for physician labeling
Accelerating Availability of New Drugs for Patients with Serious Diseases

- **Accelerated Approval**
  - allows earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint

- **Fast Track**
  - facilitates the development and expedites the review of drugs to treat serious diseases and fill an unmet medical need

- **Priority Review**
  - reduces the time it takes FDA to review a new drug application
Breakthrough Therapies

- Expedited development and review of drugs that –
  - Treat serious/life-threatening disease; and
  - Preliminary clinical evidence indicates that drug may demonstrate substantial improvement over existing therapies

- Features of breakthrough therapy designation include:
  - Frequent FDA/sponsor communications & meetings
  - Cross-disciplinary project lead assigned to FDA review team
  - Organizational commitment in a proactive, collaborative, cross-disciplinary review

- Helpful resources on breakthrough therapies –
  - http://tinyurl.com/fdabt
New Drug Application (NDA) or Biologic License Application (BLA) contains the following:

- Pre-clinical studies
- Human clinical studies
- Manufacturing details
- Labeling
- Additional information
Biosimilars

- Biological products:
  - Therapies used to treat diseases and health conditions
  - Include a variety of products including vaccines, blood and blood components, gene therapies, tissues, and proteins
  - Generally are made from human and/or animal materials

- FDA issued guidance documents on biosimilars development to assist industry in developing biosimilar versions of approved biological products
Biosimilar User Fee Act (BsUFA)

- Authorizes FDA to assess and collect fees for biosimilar biological products
- FDA dedicates these fees to expediting the review process for biosimilar biological products

http://www.fda.gov/forindustry/userfees/biosimilaruserfeeaactbsufa/default.htm
Prescription Drug
User Fee Act (PDUFA)

http://www.fda.gov/oc/pdufa/default.htm

- Permits CDER/CBER to charge pharmaceutical manufacturers a fee to review drug applications
- Imposes deadlines (Standard: 10 months; Priority: 6 months)
- These fees provide appropriate resources to accelerate the review of applications
- Not the only source of funds for CDER/CBER
PDUFA V Enhancements

- **Communication**
  - “The Program”- to improve efficiency and effectiveness first cycle reviews and decrease the # of cycles to approval

- **Review Performance Goals**
  - PDUFA review clock begins later under the Program

- **Communication Liaisons (Enhanced Communication Team)**
  - Additional resource to enhance communication between FDA and sponsors during drug development
  - ONDEnhancedComm@fda.hhs.gov

- **Electronic Submissions**
  - Draft guidance available, will eventually be mandatory
  - http://tinyurl.com/esubmissions
PDUFA Fees (FY 2016)

- **Application Fee**
  - Requiring clinical data: $2,374,200
  - Not requiring clinical data: $1,187,100
  - Supplements requiring clinical data: $1,187,100

- **Establishment Fee:** $585,200

- **Product Fee:** $114,450
Advisory Committees

- Panel of OUTSIDE experts
- Provide advice and opinions to the FDA drug review team

FDA advisory committee Information:

http://www.fda.gov/AdvisoryCommittees/default.htm
NDA / BLA Review in CDER: The Final Action(s)

Complete Response (CR)

Approval (AP)
FDA Evaluates benefits/risks for the population

Provider evaluates benefits/risk for a patient

Patient evaluates benefits/risks in terms of personal values
Pre-Clinical R&D

Submit IND

Pre-IND Meeting

Phase 1

EOP2 Meeting

Phases 2, 3

Pre-NDA/BLA Meeting

FDA Review

AC Meeting

Post-marketing Commitments

Phase 4

Labeling & Risk Evaluation Meetings

SAFETY

EFFICACY
Post-marketing Activities

- Safety/adverse reaction surveillance
- Product defect reporting
- Marketing and advertising
- Compliance
- Post-approval inspections
Financial Incentives

- Grants
- Orphan Designation
- Orphan Products Grants Program
- PDUFA Waivers
Grants

- Solicited grant applications
  - Solicited through RFAs posted at http://grants.gov
  - http://tinyurl.com/FDAgrants

- Unsolicited grant applications
  - Applications not submitted in response to an RFA; submitted to NIH (Center for Scientific Review)

- SBIR/STTR

- NIH grants and funding opportunities
Orphan Drugs

- For Rare Diseases and Conditions
  - Less than 200,000 persons
  - No expectation of development cost recovery

- Incentives
  - Waiver of PDUFA application and supplement fees
  - Tax credit for clinical research
  - 7 years market exclusivity (vs. 5 years)

- Designation
  - Administered by Office of Orphan Products Development
  - Does not alter the standard review requirements
Orphan Grants Programs

- Orphan Products Grants Program
  - Goal: to encourage clinical development of products for use in rare diseases or conditions
    - FDA provides grants for clinical studies on safety and/or effectiveness that will either result in, or substantially contribute to, market approval of these products
  - For information and application process/RFA postings:
    http://tinyurl.com/orphangrants

- NIH Office of Rare Disease Research also provides funding
  - http://tinyurl.com/NIHraredisease
PDUFA Waivers

A waiver may be granted for one or more fees where:

- a waiver or reduction is necessary to protect the public health;
- assessment of the user fees would present a significant barrier to innovation due to limited resources or other circumstances;
- the fees will exceed the anticipated present and future costs incurred by FDA for conducting the process for the review of the new drug applications for the person;
- The applicant is a small business submitting its first human drug application to the Secretary for review.
PDUFA Waiver for Small Business

To qualify for a small business waiver, an applicant must meet all of these criteria:

- Employs fewer than 500 employees, including affiliates;
- Does not have a drug product that has been approved under a human drug application and introduced or delivered for introduction into interstate commerce; and
- The applicant, including its affiliates, is submitting its first human drug application.

Guidance for Industry User Fee Waivers, Reductions, and Refunds for Drug and Biological products (03/11/11)
http://tinyurl.com/WaiversGuidance

FAQs:
http://tinyurl.com/PDUFAFAQs
Thank You!

Telephone: 1.866.405.5367 or 301.796.6707

Email: CDERSBIA@fda.hhs.gov

Web-Site: http://www.fda.gov/cdersbia

- Sign up for the CDER SBIA Listserv on our website
References

- CDER SBIA: [http://www.fda.gov/CDERSBIA](http://www.fda.gov/CDERSBIA)
- CDER Enhanced Communication Team: [http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm327281.htm](http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm327281.htm)