The New Drug Approval Process: NDA Submission and Review

Elizabeth Mulkey

April 21, 2021

Roadmap

A. Content and Organization of a Full NDA

B. The Review Process

C. Expedited Programs

D. Responses to FDA Adverse Decision

E. Post-approval Study and Surveillance Requirements

F. Critical Path Innovations

Purpose of an NDA

- **Enables FDA to determine:**
  - **Whether the drug is safe and effective for the proposed indication, and whether the drug's benefits outweigh the risks**
  - **Whether the drug's proposed labeling is appropriate, and what should be included in the package insert**
  - **Whether manufacturing methods & quality controls are adequate to preserve drug's identity, strength, quality & purity**

Package Insert

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DEFITELIO safely and effectively. See full prescribing information for DEFITELIO.

DEFITELIO (defibrotide sodium) injection, for intravenous use
Initial U.S. Approval: 2016

INDICATIONS AND USAGE

DEFITELIO is indicated for the treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT). (1)

DOSAGE AND ADMINISTRATION

- Administer DEFITELIO 6.25 mg/kg every 6 hours given as a 2-hour intravenous infusion. (2.1)
- Treat for a minimum of 21 days. If after 21 days signs and symptoms of VOD have not resolved, continue treatment until resolution. (2.1)

DOSAGE FORMS AND STRENGTHS

Injection: 200 mg/2.5 mL (80 mg/mL) in a single-patient-use vial. (3)

CONTRAINDICATIONS

- Concomitant administration with systemic anticoagulant or fibrinolytic therapy. (4)
- Known hypersensitivity to DEFITELIO or to any of its excipients. (4)

WARNINGS AND PRECAUTIONS

- Hemorrhage: Monitor patients for bleeding. Withhold or discontinue DEFITELIO if significant bleeding occurs. (2.3, 5.1)
- Hypersensitivity Reactions: If severe or life threatening allergic reaction occurs, discontinue DEFITELIO, treat according to standard of care, and monitor until signs and symptoms resolve. (2.3, 5.2)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥10% and independent of causality) with DEFITELIO treatment were hypotension, diarrhea, vomiting, nausea and epistaxis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Jazz Pharmaceuticals, Inc. at 1-800-520-5568 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

- DEFITELIO may enhance the activity of antithrombotic/fibrinolytic drugs. (7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 03/2016

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

GOODWIN

A. Content & Organization of a Full NDA

- **Sources:**
  - **FDCA § 505(b)(1)**
    - High level description of NDA elements
  - **21 CFR Part 314 (i.e., 21 CFR 314.50)**
    - Detailed description of NDA elements
  - **FDA Guidance Documents**
    - Various guidance documents describe the NDA elements in much greater detail

Content of an NDA

- **Cover Letter**
  - Not officially part of the NDA content and format
  - Vitally important
  - Opportunity to give overall strategy and remind FDA of important events that occurred during development
- **Summary**
  - General understanding of the application
  - Annotated labeling text identifying supporting information from technical section of NDA
- **Chemistry, Manufacturing, and Controls (CMC)**
  - Drug substance and drug product

Content of an NDA

- **Non-Clinical Data**
  - **Animal and *in vitro* studies**
    - Pharmacology/toxicology
    - Statement of compliance with GLPs
- **Pharmacokinetics/Bioavailability**
  - In humans
- **Microbiology**
  - Only for anti-infectives

Content of an NDA

- **Clinical Data**
  - Description and analysis of studies
  - Summary of efficacy and safety
  - Benefits outweigh risks
  - Safety updates

- **Statistical**
  - Description of statistical analysis to evaluate the data

Content of an NDA

- **Pediatric Use**
  - Pediatric rule (requiring pediatric assessment unless waived or deferred)
- **Samples and Labeling (and Packaging, if Requested by FDA)**
  - FDA validation of analytical procedures
  - Labeling (package insert and patient labeling)
- **Case Report Forms**
  - Tabulations of clinical data
  - Case report forms for deaths, adverse events

Content of an NDA

- **Patent Information**
  - Information for Applicant's own patents (21 CFR 314.54)
  - Certification for other patents (21 CFR 314.50(h))
  - No process patents
  - *Note:*
    - NDA patent information is provided in FDA's "Approved Drug Products with Therapeutic Evaluations" (i.e., the "Orange Book")

- **Disclosure/Certification**
  - Investigator financial certification
  - Debarment certification
  - Claimed exclusivities
  - Compliance with clinical trial disclosure requirements

GOODWIN

Drug Master Files (DMFs)

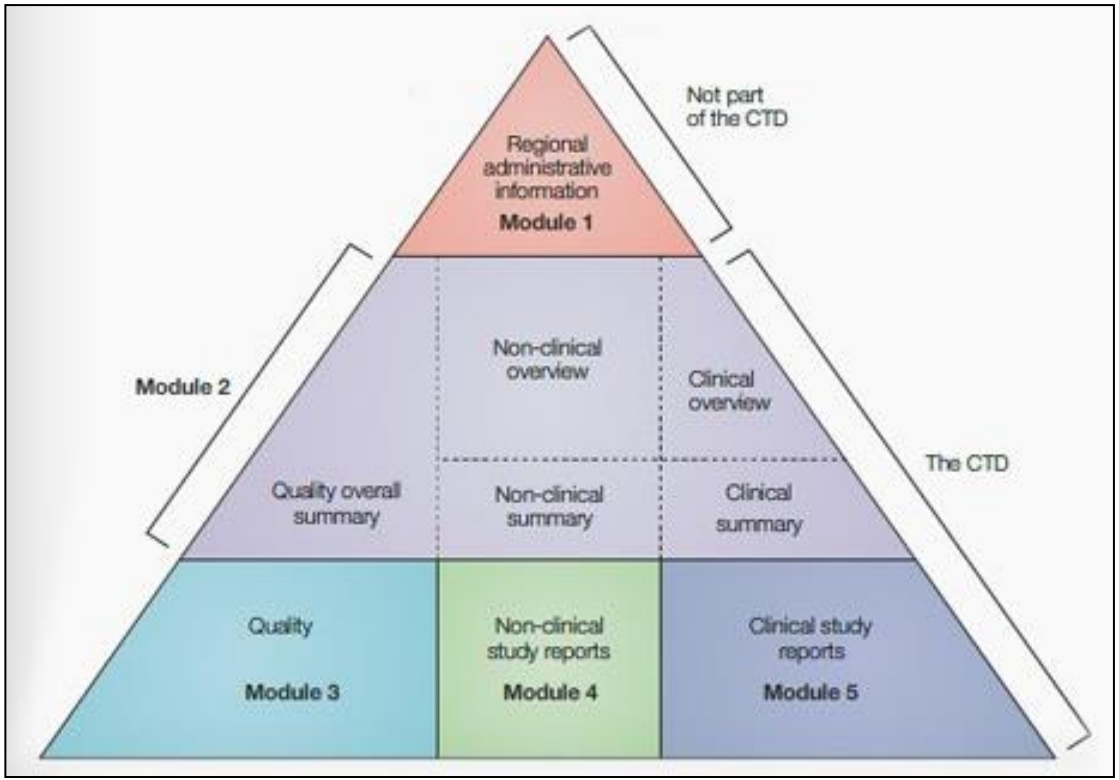
- **Submission to FDA of information concerning facilities, processes, or ingredients for a drug**
- **Method for supplying information in a confidential manner**
- **May be referenced by "DMF holder" or others (with permission) in an application (e.g., IND, NDA, or ANDA)**
- **<u>DMF Types:</u>**
  - **Type II:** Drug substance
  - **Type III:** Packaging materials
  - **Type IV:** Inactive ingredients
  - **Type V:** FDA-Accepted Reference Information

Website:
https://www.fda.gov/drugs/forms-submission-requirements/drug-master-files-dmfs
Guidance:
https://www.fda.gov/drugs/guidances-drugs/drug-master-files-guidelines
Regulation:
21 CFR 314.420

Use of the Common Technical Document (CTD)

- **CTD is a set of specs for regulatory applications & related submissions**
- **Harmonizes technical documentation for US, Europe, and Japan**
- **Int'l Conference on Harmonization (ICH)**
- **Five main modules:**
  - (1) Administrative Information
  - (2) Overviews and Summaries
  - (3) Quality (pharmaceutical documentation)
  - (4) Non-Clinical Reports (pharmacology/toxicology)
  - (5) Clinical Study Reports (clinical trials)

The 5 CTD Modules



GOODWIN

Electronic Common Technical Document (eCTD)

- **Electronic submission**
  - eCTD format is required
  - FDA eCTD Web Page:
    https://www.fda.gov/drugs/electronic-regulatory-submission-and-review/electronic-common-technical-document-ectd


Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications

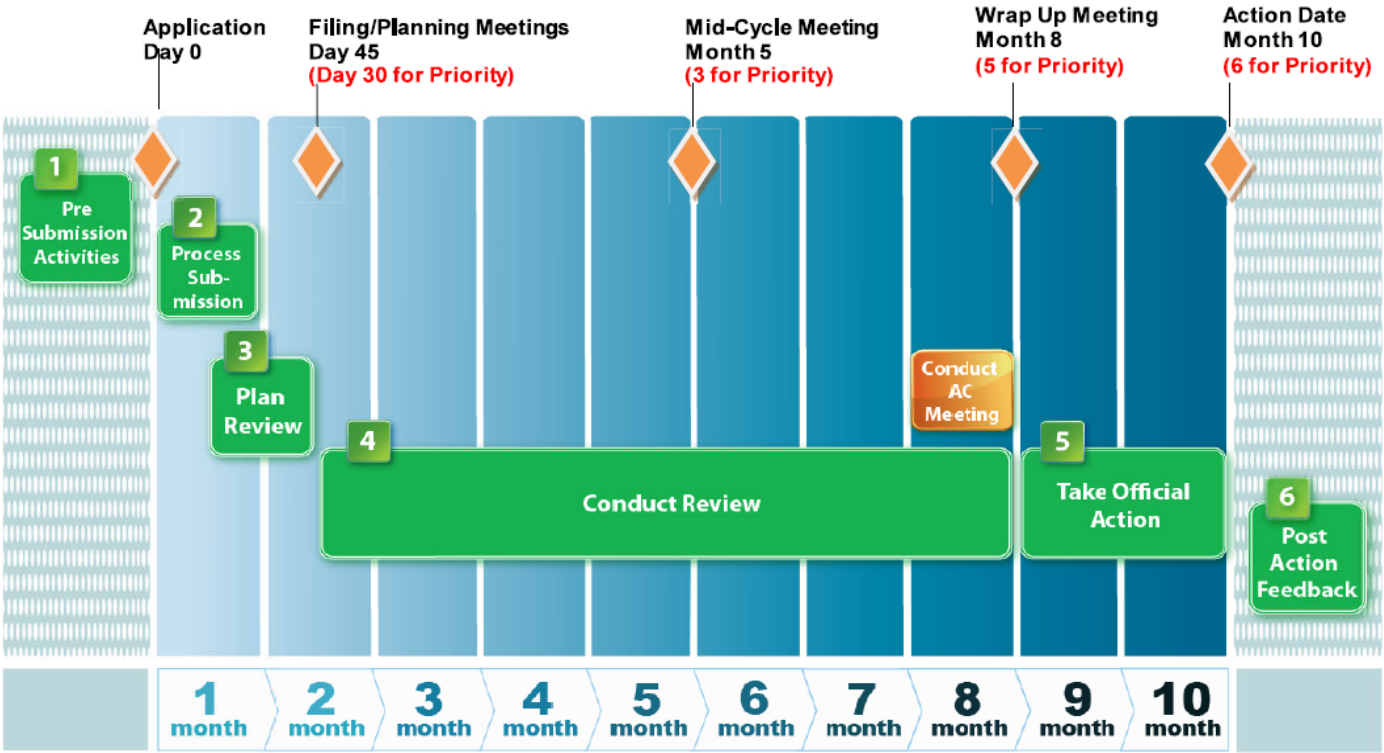
Guidance for Industry

GOODWIN

B. The Review Process

- User Fees and Goals (PDUFA)
- The Review Clock and Impact of PDUFA
- Interacting with FDA
- Pre-Approval Inspections (PAIs)
- Complete Response and Approval Letters

Overview of the NDA/BLA Review Process and Major Steps for Completing the Review



Note: The timeline for review of NMEs/BLAs under PDUFA V's "Program" Review extends the *Conduct Review* Phase by two months.

See Appendix A for a timeline diagram for PDUFA V.

GOODWIN

User Fees and Goals (PDUFA)

- **Prescription Drug User Fee Act (PDUFA) was enacted in 1992**
  - Intended to address U.S. "drug lag"
  - Reauthorized every 5 years
  - Last reauthorized in 2017 as part of FDARA (PDUFA VI)
- **Leading up to PDUFA reauthorization, FDA and stakeholders negotiate goals**
- **PDUFA outlines the "user fees" drug sponsors must pay for FDA activities related to prescription drug reviews**
  - Application Fees
  - Program Fees
- **FDA agrees to user fee "goals" for review timelines and additional goals or programs (e.g., patient-focused drug development meetings)**
  - During the COVID-19 pandemic, FDA has continued to publish updates on its ability to meet these goals

PDUFA VI User Fees (FY 2021)

Fee category	Fee rates for FY 2021
Application:	
Requiring clinical data	$2,875,842
Not requiring clinical data	1,437,921
Program:	336,432

PDUFA VI User Fee Goals (FY18-22)

Table 1: Original and Resubmitted Applications and Supplements:

SUBMISSION COHORT	STANDARD	PRIORITY
NME NDAs and original BLAs	90% in 10 months of the 60 day filing date	90% in 6 months of the 60 day filing date
Non NME NDAs	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmissions	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmissions	90% in 6 months of the receipt date	90% in 6 months of the receipt date
Original Efficacy Supplements	90% in 10 months of the receipt date	90% in 6 months of the receipt date
Class 1 Resubmitted Efficacy Supplements	90% in 2 months of the receipt date	90% in 2 months of the receipt date
Class 2 Resubmitted Efficacy Supplements	90% in 6 months of the receipt date	90% in 6 months of the receipt date

Table 2:

	PRIOR APPROVAL	ALL OTHER
Manufacturing Supplements	90% in 4 months of the receipt date	90% in 6 months of the receipt date

Interacting with FDA

- **Premarket Review/Good Review Management Principles**
- **Special Protocol Assessment (SPA)**
- **Approval Meetings; Product Application Meetings**
- **Advisory Committees**

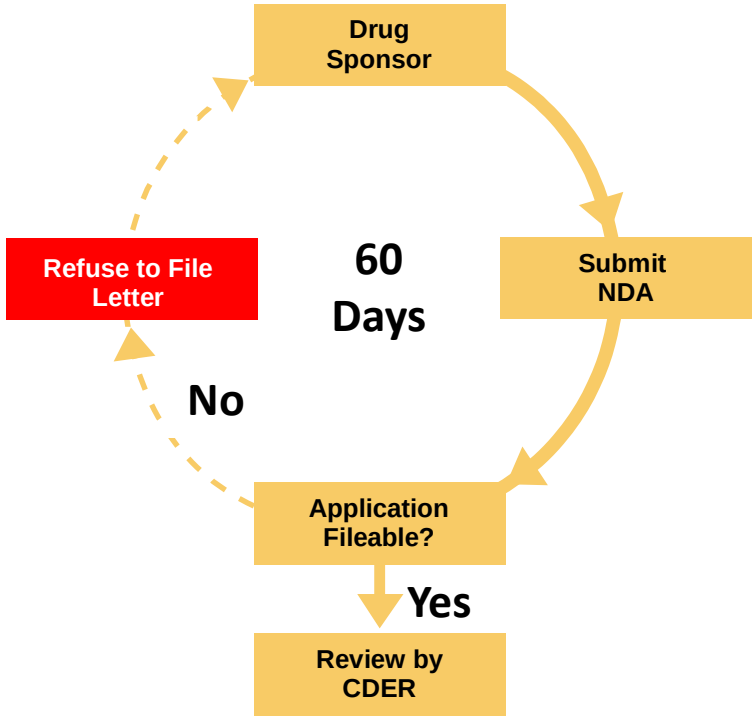
Premarket Review/ Good Review Management Principles

- **Clarify roles and responsibilities of review staff in managing the review process**

- **Identifies principles and time goals for review and action on drug applications**
  - 1. Filing Determination & Review Planning Phase
  - 2. Review Phase
  - 3. Advisory Committee Meeting Phase
  - 4. Action Phase:
    - Wrap-Up, Labeling, Signatory Review Documentation, Regulatory Action
  - 5. Post-Action Phase

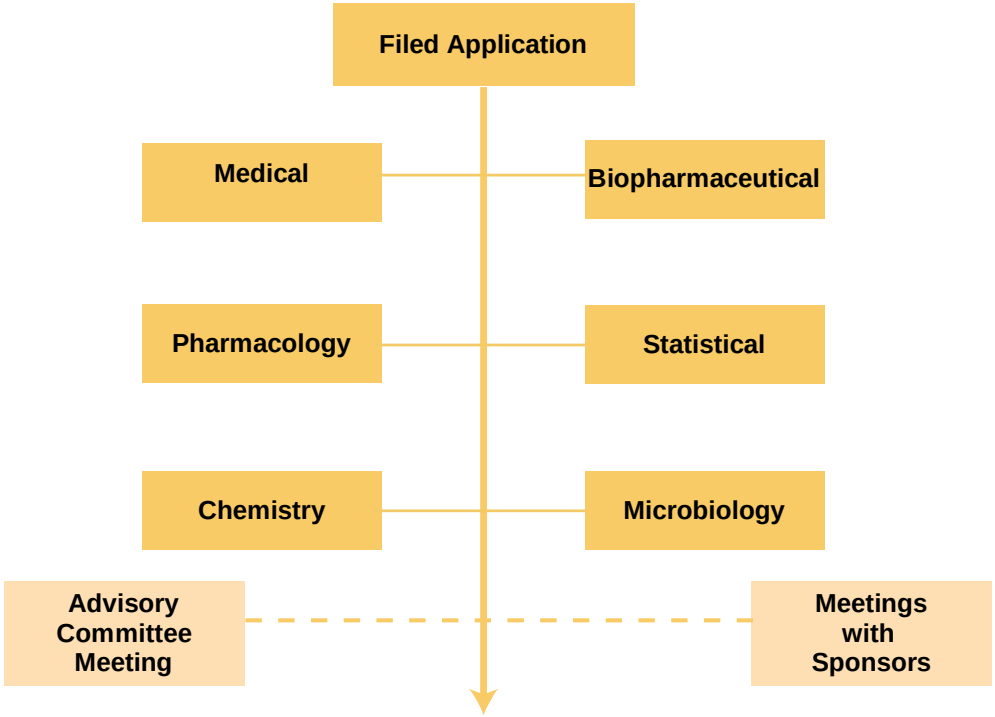
Guidance: https://www.fda.gov/media/72259/download

Reviews and Review Clocks



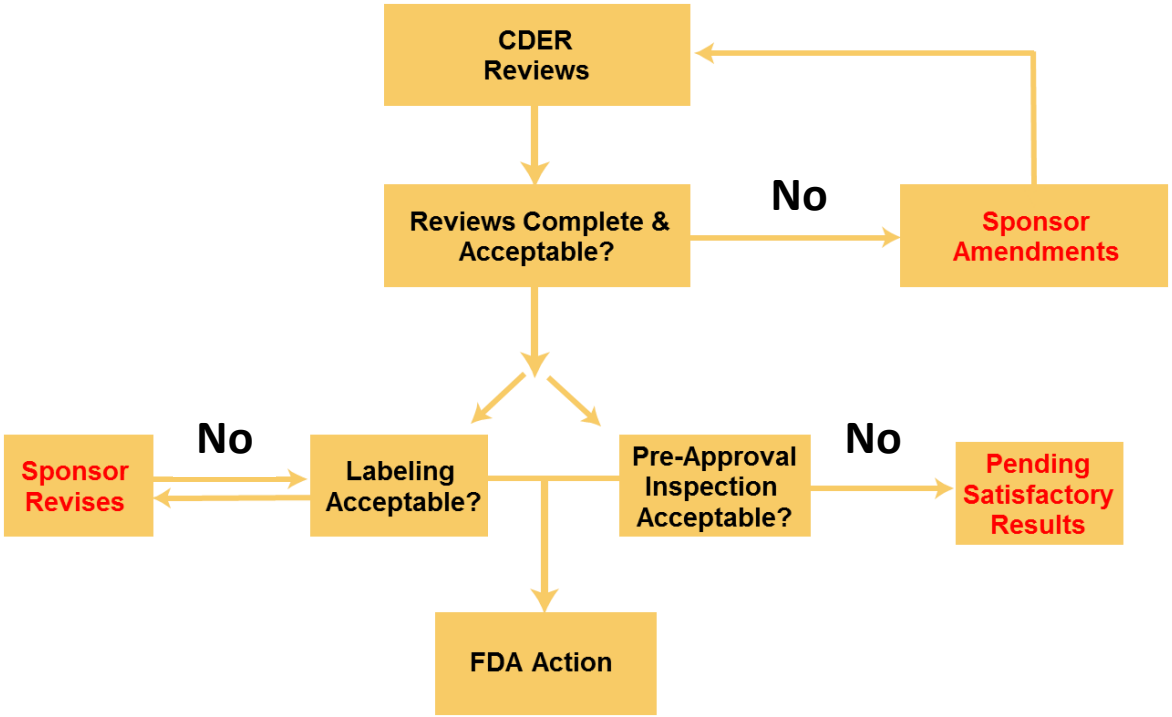
GOODWIN

Reviews and Review Clocks



GOODWIN

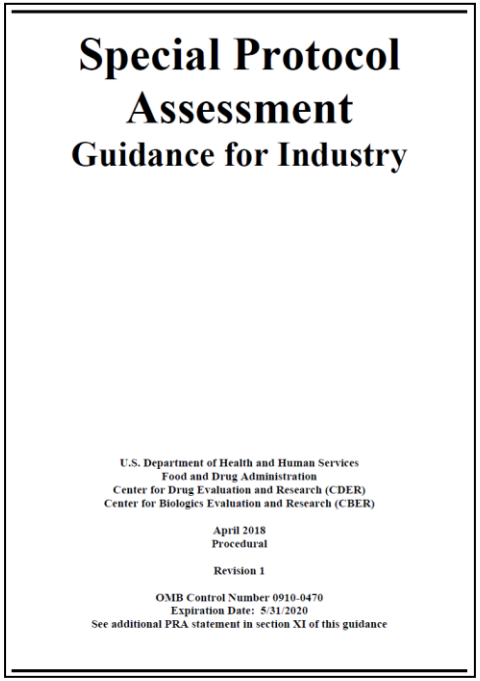
Reviews and Review Clocks



GOODWIN

Special Protocol Assessment (SPA)

- **Mechanism for requesting feedback from FDA on:**
  - Protocols
    - I.e., animal carc., final product stability, Phase 3 clinical trials
  - Whether protocols are adequate to meet scientific and regulatory requirements identified by the sponsor
- **45-day PDUFA review clock**
- **SPA agreement may be rescinded**
  - "FDA may rescind an SPA agreement when the division director or senior management determines that a substantial scientific issue essential to determining the safety or efficacy of the product has been identified after the trial has begun."
  - FDA states that less than 1% (of 1,000+) have been rescinded


Special Protocol Assessment
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

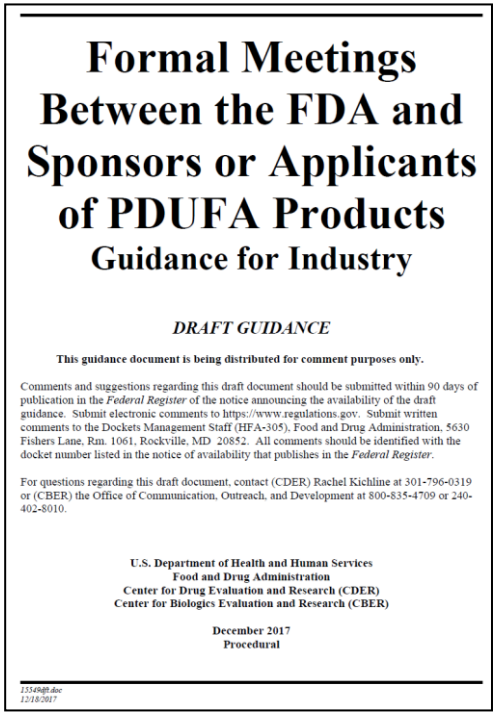
April 2018
Procedural

Revision 1

OMB Control Number 0910-0470
Expiration Date: 5/31/2020
See additional PRA statement in section XI of this guidance

Approval Meetings; Product Application Meetings

- **Sponsors may request meetings with FDA**
  - FDA grants meetings unless “clearly unnecessary” or “premature”
- **Meeting types (Face-to-Face/TC/VTC or Written Response Only)**
  - ***Type A:*** Dispute resolution, clinical hold, protocol assessment, post-action/RTF
  - ***Type B:*** Pre-IND, Pre-NDA, REMS, BT, pre-EUA
  - ***Type B (EOP):*** End-of-Phase 2, certain EOP1
  - ***Type C:*** Other than Type A, B, or B (EOP)
- **Pre-meeting submissions (request & briefing/meeting package)**
- **Preliminary responses from FDA**
- **Memorandum of meeting**



Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Rachel Kichline at 301-796-0319 or (CBER) the Office of Communication, Outreach, and Development at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

December 2017
Procedural

13349dft.doc
12/18/2017

Table A: Meeting Management Procedural Goals

Meeting Type	FDA Response to Request	FDA Receipt of Meeting Package	FDA Preliminary Responses to Requester (if applicable†)	Requester Response to FDA Preliminary Responses (if applicable†)	FDA Scheduled Meeting Date (days from receipt of request)	FDA Meeting Minutes to Requester (if applicable†)
A	14 days	With meeting request	No later than 2 days before meeting	--	Within 30 days	30 days after meeting
B	21 days	No later than 30 days before meeting	No later than 2 days before meeting	--	Within 60 days	30 days after meeting
B (EOP)*	14 days	No later than 50 days before meeting**	No later than 5 days before meeting	No later than 3 days after receipt of preliminary responses	Within 70 days	30 days after meeting
C	21 days	No later than 47 days before meeting***	No later than 5 days before meeting	No later than 3 days after receipt of preliminary responses	Within 75 days	30 days after meeting

†Not applicable to written response only.

* EOP = end of phase

** If the scheduled date of a Type B (EOP) meeting is earlier than 70 days from FDA receipt of the meeting request, the requester's meeting package will be due no sooner than 6 calendar days after FDA response time for issuing the letter granting the meeting (see Table 1 in section VI.B., Meeting Granted).

*** If the scheduled date of a Type C meeting is earlier than 75 days from FDA receipt of the meeting request, the meeting package will be due no sooner than 7 calendar days after FDA response time for issuing the letter granting the meeting. Note that for Type C meetings that are requested as early consultations on the use of a new surrogate endpoint to be used as the primary basis for product approval in a proposed context of use, the meeting package is due at the time of the meeting request.

Examples – What Type of Meeting?

[Survey: Type A / Type B / Type C]

- A sponsor has completed Phase 2 studies and is planning for Phase 3
- There is a clinical hold in place, and FDA and the sponsor agree that a new path forward should be discussed
- A sponsor wants to discuss the appropriate endpoints to be used in a rare disease trial

Advisory Committees

- **FDA generally has discretion to call advisory committee meetings**
- **FDA seeks advice for specific scientific & medical questions (e.g., re data in NDA)**
  - Advisory committees hear testimony (usually from FDA & stakeholders), discusses, and votes
  - FDA is not bound by advisory committee's vote
- **Pediatric Advisory Committee dispute resolution is the only required AdCom mtg**
- **FDCA § 505(n) describes appointment process and membership criteria**
- **Federal Advisory Committee Act (FACA)**
  - Meetings must be open to the public
  - Materials supplied to committee are public
  - Exceptions: (FOIA) trade secrets, etc.

Website: www.fda.gov/AdvisoryCommittees/
Laws, Regulation, and Guidance:
www.fda.gov/AdvisoryCommittees/AboutAdvisoryCommittees/LawsRegulationsGuidance/default.htm

Advisory Committees

View of the Dec. 20, 2012 Meeting of the Arthritis Advisory Committee

The Great Room, White Oak Conference Center, Food & Drug Administration, Silver Spring, Maryland

Source: Solve CFS

GOODWIN

Pre-Approval Inspections (PAIs)

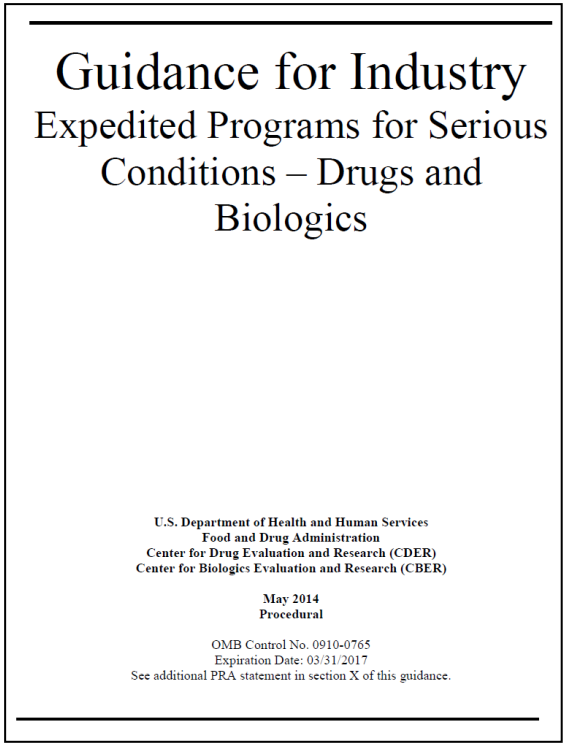
- **Goals:**
  - Ensure drug establishment is ready to manufacture the drug
  - Verify that the conformance of drug manufacturing to application specifications
  - Check the integrity of application data (data audit)
- **Application Recommendations:**
  - Withhold or Approve
- **Compliance Policy Guide 7346.832**
- **During COVID-19**
  - FDA has issued guidance on availability of remote interactive evaluations

Complete Response & Approval Letters

- **Complete Response (21 CFR 314.110)**
  - Possible reasons to refuse to approve outlined in 21 CFR 314.125 (e.g., inadequate evidence of effectiveness & safety, inadeq. CMC, inadeq. labeling)
  - **Sponsors can:**
    - Resubmit with new PDUFA review goals
    - Withdraw the marketing application
    - Request an opportunity for hearing
- **FDA Approval Letter (21 CFR 314.105)**
  - If none of the reasons to refuse to approve outlined in 21 CFR 314.125 applies
  - Marketing application may be approved if there are minor labeling deficiencies

C. Expedited Programs

- **Expedited programs:**
  - **Fast track**
  - **Priority review**
  - **Breakthrough therapy designation (also RMAT)**
  - **Accelerated Approval**
- **These programs are intended to speed the development and approval of therapies to treat serious, life-threatening diseases and conditions**
- **Competing interests:**
  - Ensuring safety & effectiveness vs. avoiding undue delay
- **Development program may be eligible for multiple expedited programs**



Guidance for Industry

Expedited Programs for Serious Conditions – Drugs and Biologics

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2014
Procedural

OMB Control No. 0910-0765
Expiration Date: 03/31/2017
See additional PRA statement in section X of this guidance.

Fast Track & Priority Review

- **Fast Track** (FDCA § 506(b))
  - For serious conditions and demonstrated potential to fill unmet medical need
  - Also available to sponsors of drugs designated by FDA as Qualified Infection Disease Products (QIDPs)
  - More FDA meetings and interactions & rolling review of application

- **Priority Review** (PDUFA)
  - For serious conditions and demonstrated potential for significant improvement in safety or effectiveness
  - Also available to sponsors that redeem priority review vouchers (tropical disease, rare pediatric disease, medical countermeasure priority review vouchers, FDCA § § 524, 529, 565A)
  - FDA reviews application within 6 months (rather than 10 months)

Breakthrough Therapy Designation

- For serious condition and preliminary evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies

- Intensive guidance on efficient drug development; organizational commitment; rolling review; other actions to expedited review (including a potentially shorter review time)

- FDCA § 506(a)

Regenerative Medicine Advanced Therapy (RMAT) Designation

- **Established by 21st Century Cures Act (FDCA § 506(g)), a drug is eligible for RMAT designation if:**
  - The drug is a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and CFR Part 1271;
  - The drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; **AND**
  - Preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition
- **Features:**
  - Expedited development and review, including early interactions with FDA to discuss surrogate or intermediate endpoints to support accelerated approval; also eligible for priority review

Accelerated Approval/Subpart H

- Unlike Fast Track, Priority Review, Breakthrough, and RMAT which reduce FDA's review time, Accelerated Approval shortens the Sponsor's clinical development time
- For serious conditions with a meaningful advantage over available therapy
- Permits the use of a "surrogate endpoint" that is likely to predict clinical benefit (e.g., viral load, tumor shrinkage)
- Sponsors required to conduct post-marketing studies to confirm benefit (i.e., confirmatory trials)
- FDCA § 506(c); 21 CFR 314.500

Designation	Fast Track	Breakthrough Therapy	Accelerated Approval	Priority Review
Timing	At submission of IND through pre-NDA/pre-BLA meeting	At submission of IND or later (preferably before EOP2 meeting); must have prelim. clinical data	No formal process; discuss with FDA during development, including use of planned endpoint and confirmatory studies	At time of submission of NDA or BLA
Eligibility	1. Serious condition, AND 2. Potential to fill **unmet medical need**	1. Serious condition, AND 2. Preliminary data → may have **substantial improvement** over existing therapies on clinically significant endpoint	1. Serious condition, AND **2.** **Meaningful advantage** over existing therapies, AND **3.** **Surrogate or intermediate endpoint** reasonably likely to predict clinical benefit	1. Serious condition, AND **2.** **Significant improvement** over existing therapies on safety or efficacy
Type of Data	**Preclinical data** is acceptable as is clinical data	Must have **clinical data**	Must have **clinical data** with a surrogate or intermediate endpoint	-

Examples – What Expedited Program?

[Survey – Fast Track / BTD / AA]

- This program involves use of a surrogate endpoint or intermediate clinical endpoint
- This designation may be granted on the basis of preclinical data
- This program is intended for a drug that treats a serious/life-threatening condition and preliminary clinical evidence indicates that it may demonstrate improvement over available therapies

D. Responses to FDA Adverse Decisions

- **Administrative Matters**
  - Consumer safety officer
  - Ombudsman

- **Scientific & Medical Disputes**
  - End-of-review meeting
  - Appeal within hierarchy under the regulations
  - Formal dispute resolution
  - Right to advisory committee review

Responses to FDA Adverse Decisions

- **Right to a Hearing on Refusal to Approve an Application**
  - Applicants have a right to an administrative hearing if FDA refuses to approve an application
  - FDCA § 505(d)

- **Judicial Review of Refusal to Approve an Application**
  - Applicants have a right to judicial review in U.S. Court of Appeals
  - Deference to scientific determinations
  - Rarely invoked
  - FDCA § 505(h)

- **Judicial Review of Approval of a Competitor's Application**
  - Extremely uncommon (if at all)

E. Post-Approval Study & Surveillance Reqts

- Risk Evaluation and Mitigation Strategies (REMS)
- Safety Labeling Changes
- Post-Approval Study Requirements
- FDAAA (Post-Approval Surveillance)

REMS

- REMS are required risk management plans that use risk minimization strategies beyond the professional labeling to ensure that the benefits of certain prescription drugs outweigh their risks

- Essentially, a REMS is a safety strategy to manage a known or potential serious risk associated with a medicine and to enable patients to have continued access to such medicines by managing their safe use

REMS

- **FDA <u>may</u> require REMS for a drug:**
  - To ensure benefits outweigh risks (new & marketed drugs) (FDCA § 505-1(a)); **<u>or</u>**
  - If "new safety information" causes FDA to determine a REMS is necessary to ensure benefits of the drug outweigh the risks (FDCA § 505-1(a)(2))

- **Information sources include:** clinical trials; epidemiological studies; adverse event reports; literature; FDA monitoring system. (FDCA § 505-1(b)(3))

REMS

- REMS must address "serious risks" (e.g., death, immediate risk of death, hospitalization, incapacity, birth defects)
- REMS can be required for a single drug or a class of drugs
- FDA will generally inform a company that REMS are required; companies then submit a proposed REMS (FDCA § 505-1(a)(1))
- Disagreements are handled through a dispute resolution procedure (FDCA § 505-1(h))
- FDA can enforce REMS as statutory violations (FDCA § 505(p))

REMS

- **Companies must submit written assessments to FDA at predefined intervals (FDCA § 505-1(d)-(g))**
- **REMS may be modified, added, or removed (FDCA § 505-1(g)-(h))**
- **Existing REMS apply to generic versions, with limitations (FDCA § 505-1(i))**

REMS Elements

- **Medication Guide to Patients (FDCA § 505-1(e)(2))**
- **Communications to Health Care Professionals (FDCA § 505-1(e)(3))**
- **Elements to Assure Safe Use (ETASU) (FDCA § 505-1(f)(3))**
  - For drugs with "inherent toxicity" or potential harmfulness
  - ETASU "elements" must be commensurate with the specific, serious risk & not unduly burdensome on patient access
  - *May include:*
    - Physician training programs; pharmacy certification; central pharmacy distribution; restrictions on use settings; patient registry enrollment; specific patient monitoring

Safety Labeling Changes

- **FDA may require safety labeling changes for already approved drugs (FDCA § 505(o)(4))**
  - Criterion:
    - Whether new safety info "should be included" in the labeling
  - Sponsors are notified by FDA
  - Sponsors submit labeling changes in a supp'l appl'n
  - Failure to comply is a statutory violation

Post-Approval Study Requirements

- **FDA may require post-approval safety studies**
  - FDA may only require post-approval safety studies if adverse event reporting and active post-market risk identification and analysis system are inadequate to assess drug risks
  - FDCA § 505(o)(3)(D)
- **Purpose of studies**
  - Assess known, serious risk; signals of serious risk; or identify an unexpected serious risk when available data indicates the potential for a serious risk
  - FDCA § 505(o)(3)(D)
- **FDA may impose post-approval study requirements on basis of "new safety information"**
  - FDCA § 505(o)(3)(C)

Post-Approval Surveillance

- **FDA Sentinel Initiative**
  - Public/private effort led by FDA & Center for Medicare & Medicaid Services (CMS)
  - ***Goal:*** Create "Sentinel System," an integrated, national, electronic system, for proactively tracking reports of adverse events linked to use of med. products

- **Drug Safety Website**
  - FDAAA required publicly-available labeling information, access to adverse event reports and summaries, and online submission of adverse event reports
  - https://www.fda.gov/drugs/drug-safety-and-availability/postmarket-drug-safety-information-patients-and-providers

F. Critical Path Innovation Meetings

- **Developed as means by which CDER and investigators from industry, academia, patient advocacy groups & govt can communicate to improve efficiency & success in drug dev't.**

- **Goals:**
  - (1) To discuss a methodology or technology proposed by the meeting requester; and
  - (2) for CDER to provide general advice on how this methodology/tech might enhance drug dev't.

- **Potential topics:**
  - Trial design (e.g., natural history study designs)
  - Biomarkers
  - Clinical endpoints (e.g., patient-reported outcomes)
  - Emerging technologies or new uses of existing technologies

- **Stakeholders may submit a request for CPIM**

Guidance:
https://www.fda.gov/regulatory-information/search-fda-guidance-documents/critical-path-innovation-meetings
Policy and Procedures:
http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM422216.pdf

Thank You

Questions?

EMulkey@goodwinlaw.com

GOODWIN