Overview of FDA Expedited Programs with a Focus on Breakthrough Therapy

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Overview

- FDA Expedited Programs
- Breakthrough Therapy Designation(BTD)
  - The BTD Request Process
  - BTD: Drug Development
  - BTD: Marketing Application Review
  - Current BTD Numbers
- Resources for Industry

FDA Expedited Programs

- ***Guidance to Industry: Expedited Programs for Serious Conditions – Drugs and Biologics***, issued May 2014
  - Single resource for information on FDA's policies & procedures for 4 expedited programs
  - Describes threshold criteria applicable to concluding that a drug is a candidate for an expedited development & review program

Expedited Programs: Goals

- For drugs that address an unmet medical need in the treatment of a serious or life-threatening condition
- Intended to help ensure that therapies for these conditions are approved & available to patients as soon as it can be concluded that the therapies' benefits justify their risks
- Allow for earlier attention to drugs that have promise in treating such conditions

Four Expedited Programs

- **Fast Track:** Section 506(b) of FD&C Act added by section 112 of the Food and Drug Administration Modernization Act of 1997 (FDAMA), amended by section 901 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA)
- **Breakthrough Therapy Designation**: Section 506(a) of the FD&C Act, as added by section 902 of FDASIA, 2012
- **Priority Review**: Prescription Drug User Fee Act of 1992
- **Accelerated Approval:** Section 506(c) Food, Drug & Cosmetic Act (FD&C Act) of the FD&C Act of 1992, amended by section 901 of FDASIA

Fast Track

- Criteria:
  - A drug that:
    - Is intended to treat a serious condition **AND** nonclinical or clinical data demonstrate the potential to address unmet medical need **OR**
    - That has been designated as a qualified infectious disease product
- Features:
  - FDA takes actions to expedite development and review
  - Eligible for rolling review

Breakthrough Therapy Program

❖ Criteria

- A drug that treats:
  - Serious condition, AND
  - Preliminary clinical evidence indicates that the drug may demonstrate **substantial** improvement over available therapy on one or more clinically significant endpoints

❖ Features

- Intensive guidance on efficient drug development
- Organizational commitment
- Eligible for rolling review

Priority Review

❖ Criteria:

- An application for a drug :
  - That treats a serious condition AND, if approved, would provide a significant improvement in safety or effectiveness OR
  - That proposes a labeling change pursuant to a report on a pediatric study under 505A OR (supplements only)
  - That has been designated as a qualified infectious disease product OR
  - Submitted with a priority review voucher

❖ Features:

- Shorter clock for review of marketing application compared with standard review

Accelerated Approval

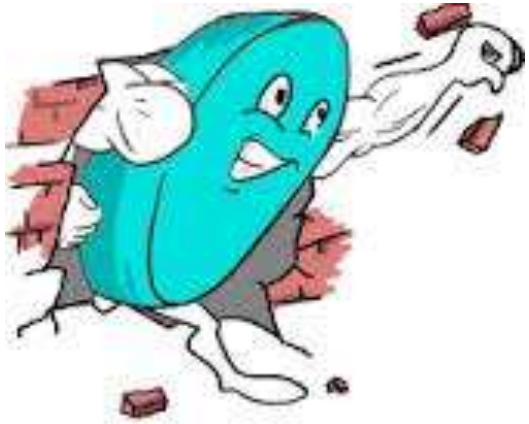
❖ Criteria:

- A drug that:
  - treats a serious condition AND ,
  - provides meaningful advantage over available therapies AND
  - demonstrates effect on surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM) that is reasonably likely to predict an effect on IMM or other clinical benefit

❖ Features:

- Approval based on an effect on surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict drug's clinical benefit

The CDER Breakthrough Therapy Program



BTD Request Submissions

- BTD requests (BTDRs):
  - Can be submitted with an original IND or any time thereafter
  - Ideally submitted prior to initiation of clinical trial(s) intended to serve as primary basis for demonstration of efficacy
  - Must include preliminary clinical evidence
  - Each indication requires a separate BTDR

CDER Review of BTDRs

- 60 day review clock
- Review Division (RD) takes the lead on reviewing BTDRs
- All BTDRs also reviewed by the Medical Policy Council (MPC) to insure statutory provisions are implemented consistently
- RD makes recommendation to the MPC to grant or deny BTDR
- MPC & RD discuss & determine final BT designation

FDASIA 902 Requirements

- FDASIA 902 states that <u>once a BTD granted</u>:
  - FDA will take actions to **expedite the development & review of the drug:**
    - Assign a cross-disciplinary project lead **(CDPL)**
    - **Hold meetings** with the sponsor throughout drug development
    - Provide timely **advice to & interactive communication** with the sponsor
    - Take steps to **ensure efficient clinical trial design**
    - **Involve senior managers** & experienced review staff

*Food and Drug Administration Safety and Innovation Act

Cross Disciplinary Project Lead

CDPL

Acts as a Scientific Liaison between all members of review team

Addresses & facilitates Issue resolution

Keeps management apprised of BT program status & progress

CDER-Sponsor Meetings

- Initial Comprehensive Multidisciplinary BT meeting
  - Type B meeting
  - Ideally scheduled within 6 months of granting
  - Comprehensive high-level discussion of the expedited development program
    - Planned clinical trials to generate substantial evidence to support accelerated or regular approval
    - Plans for expediting the manufacturing development strategy
    - Expanded Access programs, if applicable
    - Proprietary Name

CDER-Sponsor Meetings-2

- Subsequent Type B Meetings
  - Review team continues to meet w/sponsor throughout IND phase
  - Focused meetings to discuss specific development program data, milestones, and issues
- Critical Milestone Meetings
  - Likely to take place in at earlier time points in drug development

CDER-Sponsor Communications Outside of Formal Meetings

- Informal telecons, information requests, & emails used as tools for focused discussions, rapid information exchange, & issue resolution
- Inquiries from sponsors
  - RPMs communicate anticipated timeline for a response, based on inquiry complexity
  - CDER responds within a few days; 30 days max

Breakthrough Therapies Considerations: Drug Development

Clinical

- Trial design flexibility/innovative approaches
- Compressed drug development options
- Consideration for accelerated approval

Product Quality

- Expediting manufacturing development strategy
- Novel risk mitigation strategies
- Early facilities information

Regulatory

- Proprietary name request plans
- Potential post-approval studies
- Expanded access plans

CDER Review of BT Drug Development Programs

- Most submissions reviewed in 60 days or less*
  - Limited types of submissions require 90 days
- Review staff perform periodic high-level reviews of BTD drug development programs
  - Performed approximately every 3 to 6 months

*Per MAPP 6030.9: Good Review Practice: Good Review Management Principles and Practices for Effective IND Development and Review

Rescinding a BTD

- Review team periodically evaluates clinical evidence
- If BTD criteria are no longer met, CDER may rescind
- Intent to Rescind letter sent to sponsor
  - Sponsor has opportunity to provide additional data & rationale and/or request a meeting
- If determined BTD criteria continue to be met:
  - Plans for development of the drug discussed & communicated to sponsor
- If determined BTD criteria no longer met:
  - Designation is rescinded

Expedited Review - Marketing Applications

- CDER staff will consider an Expedited Review (ER) for each marketing application (MA) for BTD drugs
- ERs are:
  - A subset of priority reviews, and
  - Action is planned for at least one month prior to PDUFA goal date, if:
    - No unexpected review issues arise
    - Review team does not experience unexpected shift in work priorities or staffing

CDER-Sponsor Meetings & Interactions: Expedited Review

- Early dialog on timing of planned MA submission
- Intent to conduct ER discussed at MA pre-submission meeting
- "Program"-related meetings occur earlier in review cycle
- Frequent discussions and exchange of information
- Rapid issue identification & resolution

Breakthrough Therapies Considerations: Marketing Application Review

Inspections

- Early submission of clinical site data sets
- Early communications re: planning & conduct
- Activities scheduled early in review

Product Quality

- Stability data options
- Innovative steps to insure product readiness for marketing
- Flexibility on planned late amendments

Regulatory

- Expedited review
- Rolling review encouraged & submissions reviewed early
- Increased use of post-marketing commitments and requirements

Advisory Committee Meetings

- AC meetings typically are not convened
  - BTD drugs generally have an acceptable:
    - Safety profile for indication
    - Clinical trial design & endpoints
  - Applications typically do not raise:
    - Unexpected efficacy issues
    - Significant public health questions
- Need for an AC evaluated on a case-by-base basis, and may be required

Senior Management Involvement

- Subordinate & Super-office* directors stay abreast of the status of BTD drugs and provide guidance through:
  - 1:1 meetings with CDPLs
  - Administrative rounds
  - Internal meetings with leadership teams
- Medical Policy Council
  - BT Policy Meetings
  - Quarterly BTD Portfolio Reviews
  - BT Rescinding Meetings

*Super Office: An office that reports to the CDER Director and to which subordinate offices report. Subordinate Office: An office that reports to a super office.

Breakthrough Numbers*

Year	Requests	Granted	Denied	Rescinded	Approvals**
2015	87	25	37	4	9
2014	96	31	51	0	14
2013	92	31	52	0	3
2012	2	1	1	0	0

*As of 9/4/15

**Approvals for calendar year; all others for fiscal year

Resources for Industry

- MAPP 6025.6: Good Review Practice: Management of Breakthrough Therapy-Designated Drugs and Biologics

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/default.htm

- MAPP 6025.7: Good Review Practice: Review of Marketing Applications for Breakthrough Therapy-Designated Drugs and Biologics That Are Receiving an Expedited Review

http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/UCM437281.pdf

- Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM358301.pdf

Resources for Industry-2

- MAPP 6030.9: Good Review Practice: Good Review Management Principles and Practices for Effective IND Development and Review

http://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/manualofpoliciesprocedures/ucm349907.pdf

- Breakthrough Therapy Information on fda.gov

http://www.fda.gov/regulatoryinformation/legislation/federalfooddrugandcosmeticactfdcact/significantamendmentstothefdcact/fdasia/ucm329491.htm

- Section 902 of FDASIA

http://www.gpo.gov/fdsys/pkg/BILLS-112s3187enr/pdf/BILLS-112s3187enr.pdf

Thank You

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Questions

Please complete the session survey:

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