VERISTAT

WEBINAR PRESENTATION

LEVERAGING FDA EXPEDITED PROGRAMS FOR PRODUCT DEVELOPMENT SUCCESS

WEBINAR PRESENTATION FROM 20 SEPTEMBER 2019

An Impactful CRO,

Committed to Making a Difference

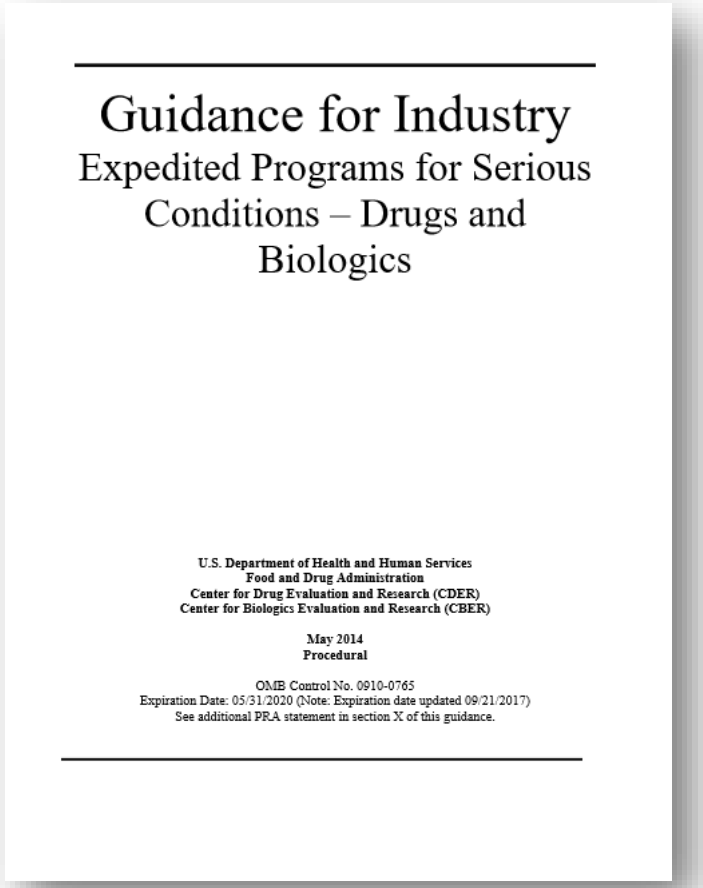
AGENDA

- FAST TRACK
- QUALIFIED INFECTIOUS DISEASE PROGRAM
- BREAKTHROUGH THERAPY
- REGENERATIVE MEDICINE ADVANCED THERAPIES
- ACCELERATED APPROVAL
- PRIORITY REVIEW

*BREAKTHROUGH DEVICE DESIGNATION
REAL-TIME ONCOLOGY PILOT REVIEW PROGRAM
ASSESSMENT AID PILOT PROJECT

FDA EXPEDITED PROGRAMS

https://www.fda.gov/media/86377/download



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: 05/31/2020 (Note: Expiration date updated 09/21/2017)
See additional PRA statement in section X of this guidance.

BENEFITS OF EXPEDITED PROGRAMS

Fast Track

- Actions to expedite development and review (opportunities for frequent interactions with the review team for a fast track product)
- Rolling review (submit documents for application in a rolling fashion)

Qualified Infectious Disease Program

- 5-year exclusivity extension
- Priority review (first application)
- Fast Track designation (must be specifically requested)

Breakthrough Therapy

- Intensive guidance on efficient drug development
- Initial Comprehensive Multidisciplinary BT meeting
- Organizational commitment
- Possibility for Expedited Review of BTD Marketing Applications (Action planned at least one month prior to PDUFA goal date)
- Rolling review

Regenerative Medicine Advanced Therapy

- All breakthrough therapy designation features, including early interactions to discuss any potential surrogate or intermediate endpoints
- Statute addresses potential ways to support accelerated approval and satisfy post-approval requirements

BENEFITS OF EXPEDITED PROGRAMS – NDA/BLA STAGE

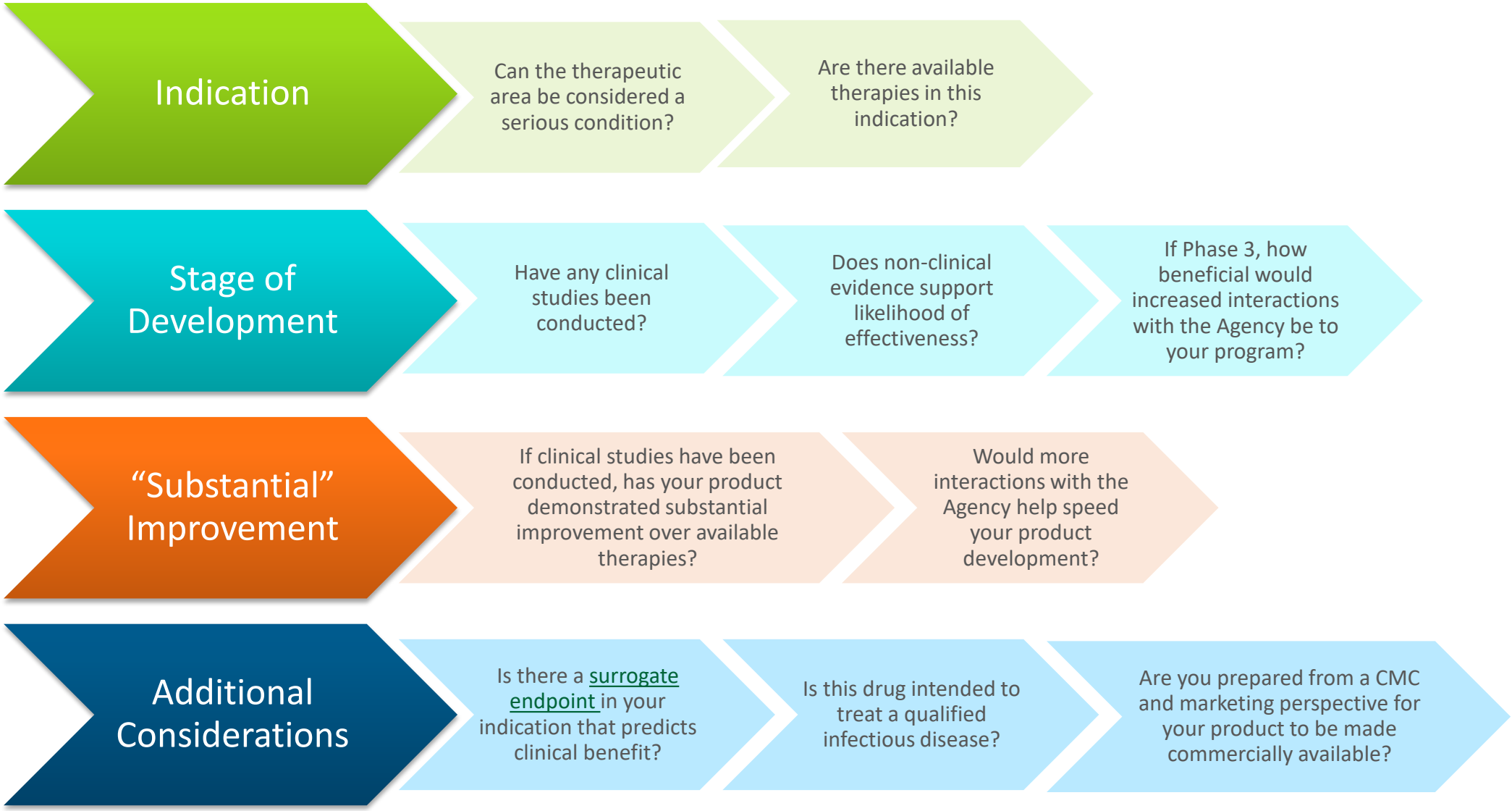
Priority Review

- Shorter clock for review of marketing application (6 months compared with the 10-month standard review)

Accelerated Approval

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

CONSIDERATIONS FOR CHOOSING PROGRAM(S)



CONCEPTS FOR EXPEDITED PROGRAMS

- Serious Condition
- Unmet Medical Need

SERIOUS CONDITION

". . . a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self- limiting morbidity will usually not be sufficient but the morbidity need not be irreversible if it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one."

Source: https://www.fda.gov/media/86377/download

AVAILABLE THERAPY – REGULATORY DEFINITION

- Is fully approved or licensed in the United States for the same indication being considered for the new drug and
- Is relevant to current U.S. standard of care (SOC) for the indication

UNMET MEDICAL NEED

WHERE THERE IS NO AVAILABLE THERAPY

WHERE THERE IS AVAILABLE THERAPY BUT THE INVESTIGATIONAL AGENT:

- ✓Has an affect on a serious outcome of the condition that is not seen with or is better than available therapy
- ✓Can be used effectively with other critical agents that cannot be combined with available therapy
- ✓ Provides efficacy comparable to available therapy while avoiding serious toxicity that occurs with available therapy, (2) avoiding less serious toxicity that is common and causes discontinuation of treatment of a serious condition, or (3) reducing the potential for harmful drug interactions
- ✓ Has a documented benefit that is expected to lead to an improvement in serious outcomes

WHERE THE ONLY AVAILABLE THERAPY was approved under the Accelerated Approval program based on a surrogate endpoint or an intermediate clinical endpoint and clinical benefit has not yet been verified

EXAMPLE INDICATIONS FOR EXPEDITED PROGRAMS

Idiopathic Pulmonary Fibrosis –

FT, then BTD granted, existing therapies slow progression, but do not halt or reverse disease, and are associated with significant adverse reactions

Metastatic Melanoma –

BTD granted based on evidence of substantial improvement in response rate and duration of response compared to existing therapies

Malaria –

BTD granted based on evidence of improved efficacy and shorter dosing regimen

BCG-unresponsive non-muscle-invasive bladder cancer (NMIBC) –

FT designation granted based on poor treatment options once BCG therapy fails

FAST TRACK

FAST TRACK DESIGNATION

Qualifying Criteria

- Serious condition
- Unmet medical need
- Nonclinical or clinical data to demonstrate the potential to address unmet medical need

FAST TRACK DESIGNATION

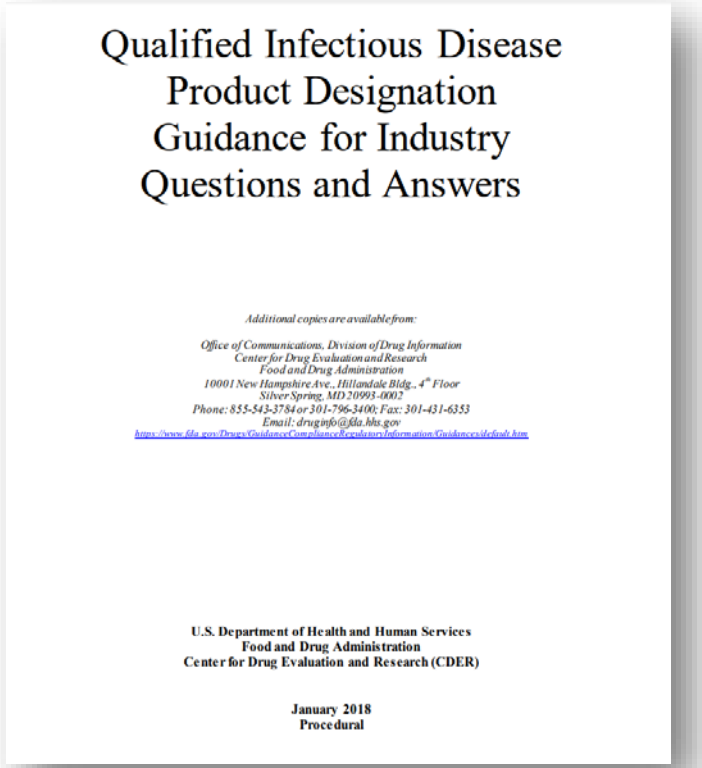
Timing and Procedure

- Submit request with IND or after; ideally no later than the pre-BLA or pre-NDA meeting
- 10-20 pages
- FDA responds within 60 days of receipt of the request
- Average Success Rate: 67.3% (March 1998-December 2018)

QUALIFIED INFECTIOUS DISEASE PROGRAM

QUALIFIED INFECTIOUS DISEASE PROGRAM

https://www.fda.gov/media/111091/download



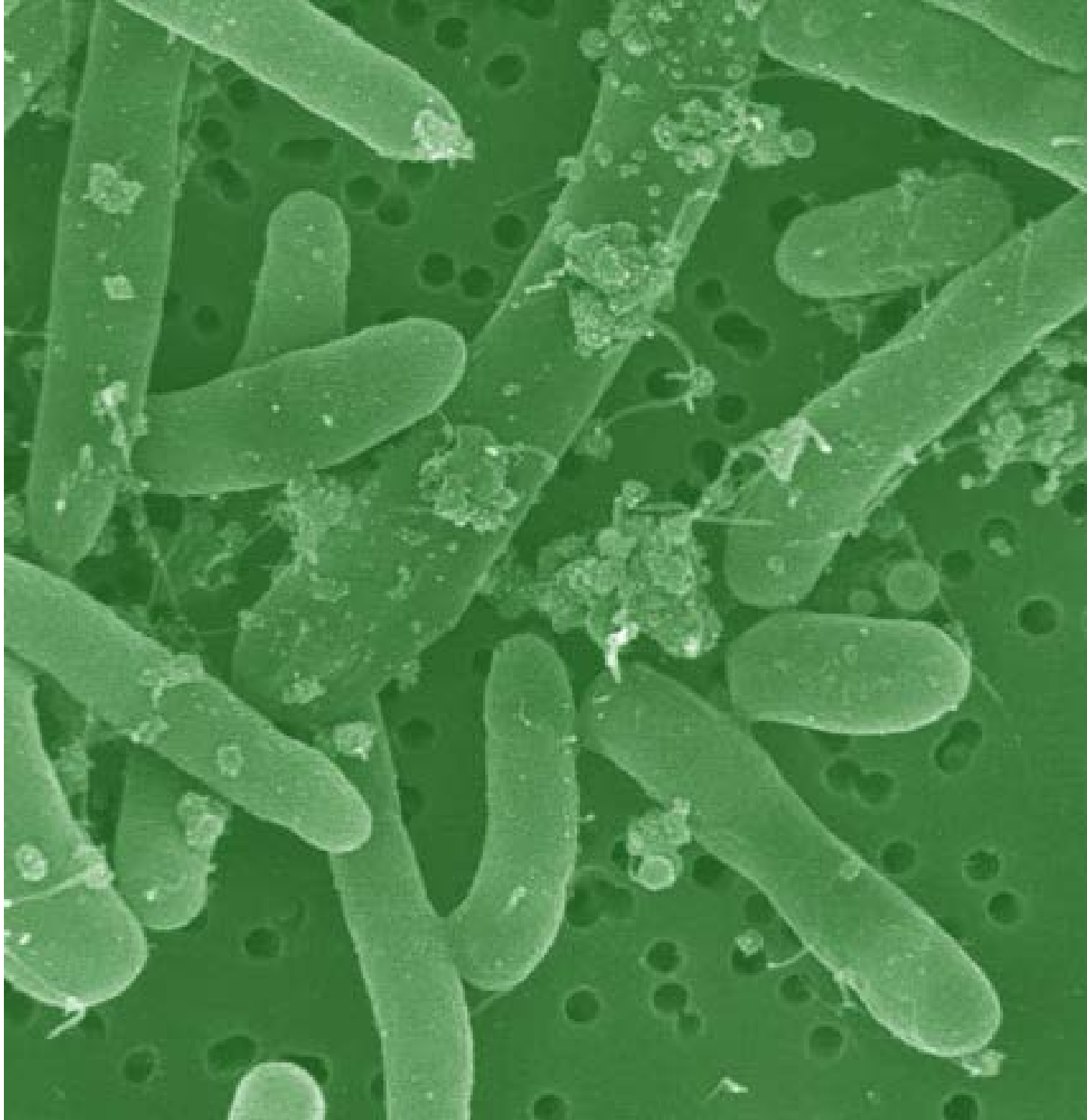
Qualified Infectious Disease Product Designation Guidance for Industry Questions and Answers

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

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

January 2018
Procedural



QUALIFIED INFECTIOUS DISEASE PROGRAM (QIDP)

Qualifying Criteria

- An antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by
  - (1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens; or
  - (2) qualifying pathogens listed in 21 CFR 317.2. Includes: *Clostridium difficile, Enterococcus* spp, *Helicobacter pylori, Mycobacterium tuberculosis, Neisseria gonorrhoeae*, *Staphylococcus aureus, Vibrio cholerae* and many others.
- Biologics and devices are not eligible for QIDP

QUALIFIED INFECTIOUS DISEASE PROGRAM (QIDP)

Timing and Procedure

- Submit request anytime prior to submission of marketing application (including pre-IND correspondence)
- Application should include specific QIDP-qualified indication, rationale for development, and data supporting antibacterial/antifungal activity (in vitro, animal model or human data)
- FDA responds within 60 days of receipt of the request

BREAKTHROUGH THERAPY

BREAKTHROUGH THERAPY DESIGNATION

Qualifying Criteria

- Serious condition
- Preliminary clinical evidence that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies

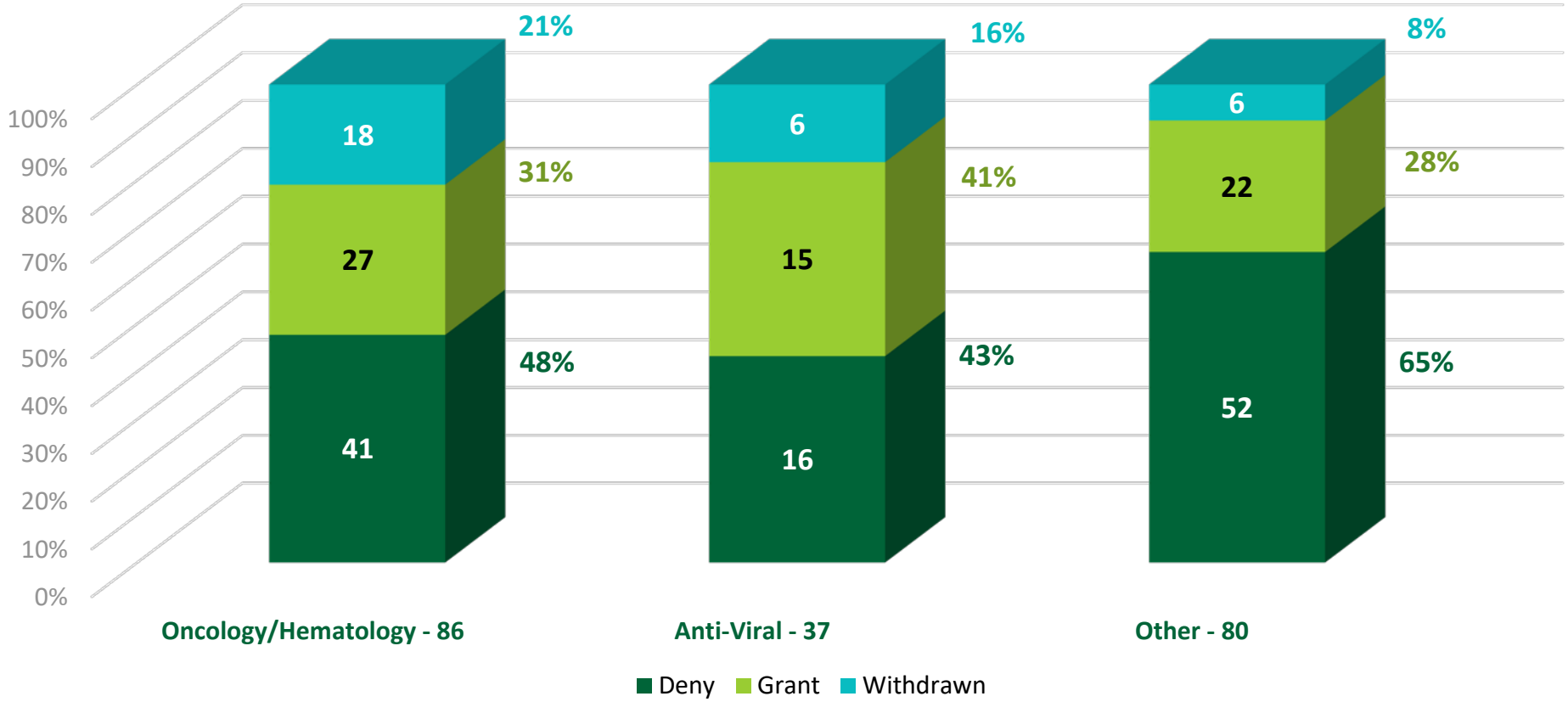
BREAKTHROUGH THERAPY DESIGNATION

Timing and Procedure

- Can be submitted with IND, but need for clinical evidence precludes this in most cases
- Ideally submitted prior to pivotal study
- FDA response in 60 days

INDICATIONS FREQUENTLY CONSIDERED FOR BTD

The majority of requests were for oncology/hematology or anti-viral drugs; antivirals had the highest proportion of grants



Source: https://www.brookings.edu/events/breakthrough-therapy-designation-exploring-the-qualifying-criteria/

BREAKTHROUGH THERAPY DESIGNATION

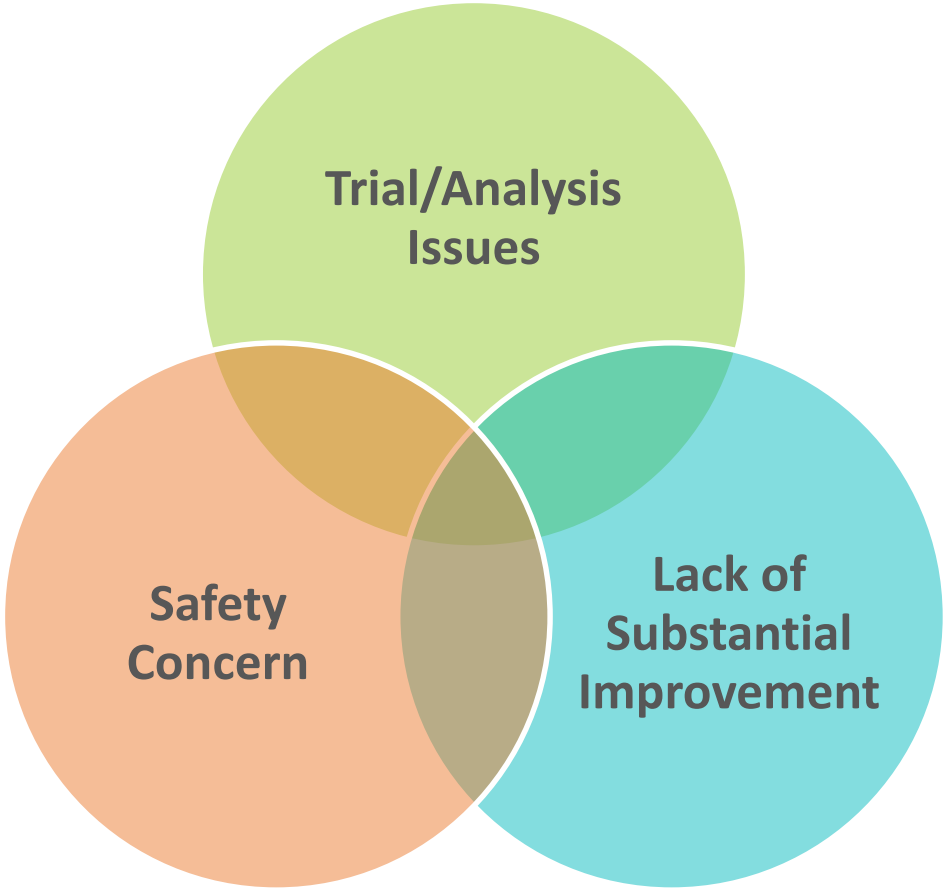
Designation Application Success Rates

FY 2013 - First Full Program	
Granted:	31 (33.7%)
Denied:	52 (56.5%)
Withdrawn:	9 (9.8%)

FY 2018	
Granted:	59 (43.4%)
Denied:	60 (44.1%)
Withdrawn:	17 (12.5%)

Source: https://www.brookings.edu/events/breakthrough-therapy-designation-exploring-the-qualifying-criteria/

BTD REASONS FOR DENIAL



Source: https://www.brookings.edu/events/breakthrough-therapy-designation-exploring-the-qualifying-criteria/

Denials N=109
Reasons for Denial*

Trial/Analysis Issues	**78 (72%)**
Trial Design Issues	45 (41%)
Sample Issues	39 (36%)
Endpoint Issues	29 (27%)
Results too preliminary	19 (17%)
Flawed post-hoc analysis	17 (16%)
Lack of Substantial Improvement	**58 (53%)**
Lack of Data	18 (17%)
No clinical data	4 (4%)
Incomplete data	14 (13%)
Safety Concerns	**12 (11%)**
Miscellaneous	14 (13%)
Not serious condition	2 (2%)
Other	12 (11%)

* Totals exceed 100% as many denials cited multiple reasons for denials.

MEETINGS WITH FDA

Initial Comprehensive Multi-Disciplinary 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 regulatory approval
  - Plans for expediting the manufacturing development strategy
  - Expanded Access programs, if applicable
  - Proprietary Name

Source: REDI presentation https://www.fda.gov/media/94063/download

OTHER COMMUNICATIONS WITH FDA

- ✓ Informal teleconference, information requests & emails used as tools for **focused discussion, rapid information exchange and issue resolution**

- ✓ Inquiries from sponsors
  - Regulatory PMs will communicate to Sponsor the anticipated timeline for a response, based on inquiry complexity
  - CDER responds with a few days, within 30 days max.

Source: https://www.fda.gov/media/94063/download

DRUG DEVELOPMENT: BTD

Clinical

Trial design/flexibility/innovative approaches

Compressed drug development options

Consideration for accelerated approval

Product Quality

Expedited manufacturing development strategy

Novel risk mitigation

Early facilities information

Regulatory

Proprietary name request plans

Potential post-approval studies

Expanded access plans

Source: REDI Presentation https://www.fda.gov/media/94063/download

EXPEDITED REVIEW

CDER staff will consider an Expedited Review (ER) for each Marketing Application (MA) for BTD drugs

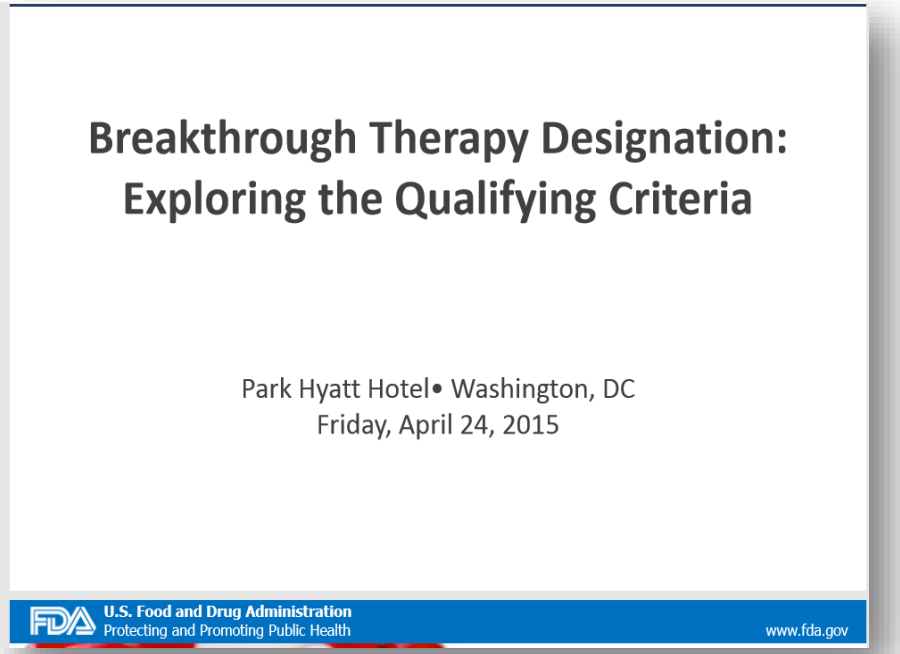
Expedited Reviews are:

- A subset of priority review, and
- Action is planned for at least one month prior to PDUFA goal date, is:
  - No unexpected review issues arise
  - Review team does not experience unexpected shift in work priorities or staffing

Source: https://www.fda.gov/media/94063/download

BREAKTHROUGH THERAPY: ADDITIONAL RESOURCES

Presentation on
"Breakthrough Therapy Designation: Exploring the Qualifying Criteria"

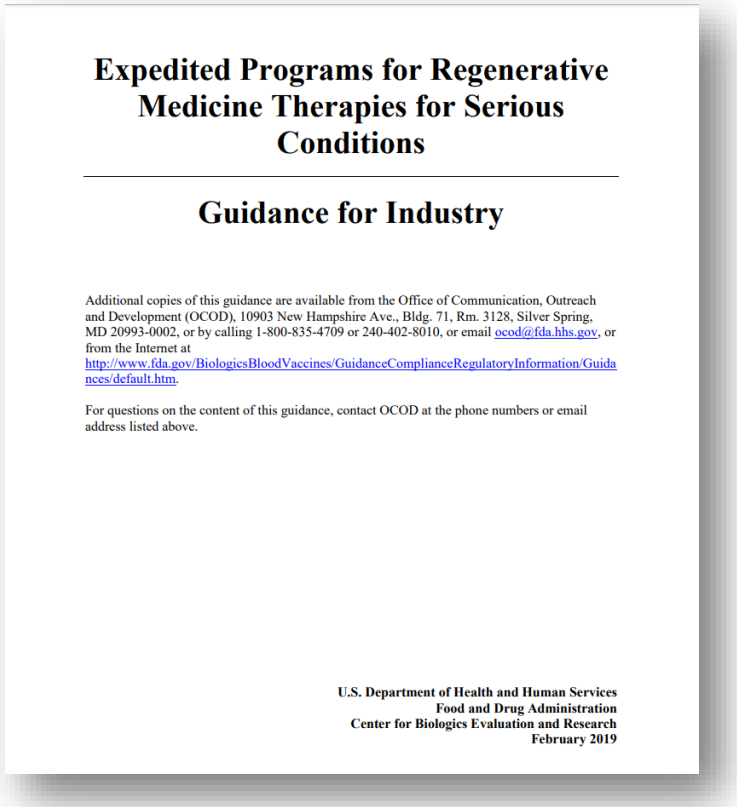


Presentation on
"Overview of FDA Expedited Programs with a Focus on Breakthrough Therapy"

REGENERATIVE MEDICINE ADVANCED THERAPY

REGENERATIVE MEDICINE ADVANCED THERAPY

https://www.fda.gov/media/120267/download



Expedited Programs for Regenerative Medicine Therapies for Serious Conditions

Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
February 2019

REGENERATIVE MEDICINE ADVANCED THERAPY

Qualifying Criteria

- Meets the definition of Regenerative Medicine
- Serious condition
- Preliminary clinical evidence indicates that the regenerative medicine therapy has the potential to address unmet medical needs for such condition
- Should be submitted at the same time as either Fast Track or Orphan Drug Designation request

REGENERATIVE MEDICINE ADVANCED THERAPY

Timing and Procedure

- Can be submitted with IND, but need for clinical evidence precludes this in most cases
- Ideally no later than EOP2 meeting
- FDA response in 60 days

MARKETING APPLICATION STAGE EXPEDITED PROGRAMS

- Priority Review
- Accelerated Approval

PRIORITY REVIEW

PRIORITY REVIEW DESIGNATION

Qualifying Criteria

- Serious condition
- If approved, would provide a significant improvement in safety or effectiveness **OR**
- Any supplement that proposes a labeling change pursuant to a report on pediatric study under 505A
- An application for a drug that has been designated as a qualified infectious disease product
- Any application or supplement for a drug submitted with a priority review voucher

PRIORITY REVIEW DESIGNATION

Timing and Procedure

- Submit request with original BLA, NDA or efficacy supplement
- FDA response in 60 days (assigned at the time of BLA, NDA or supplement filing)
- Nonclinical or clinical data to demonstrate the potential to address unmet medical need

ACCELERATED APPROVAL

ACCELERATED APPROVAL PATHWAY

Qualifying Criteria

- Serious condition
- Generally provides a meaningful advantage over available therapies **AND**
- Demonstrates an effect on a 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 that is reasonably likely to predict an effect on IMM or other clinical benefit
- Confirmatory Trial needed

ACCELERATED APPROVAL PATHWAY

Timing and Procedure

- Not a formal request – should be discussed with the review division during development

QUESTIONS ??

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