Unmet Medical Need in Antibacterial Drug Development

Expert Multi-Stakeholder Meeting

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Joseph G. Toerner, MD, MPH

Deputy Director for Safety

Division of Anti-Infective Products

CDER/FDA

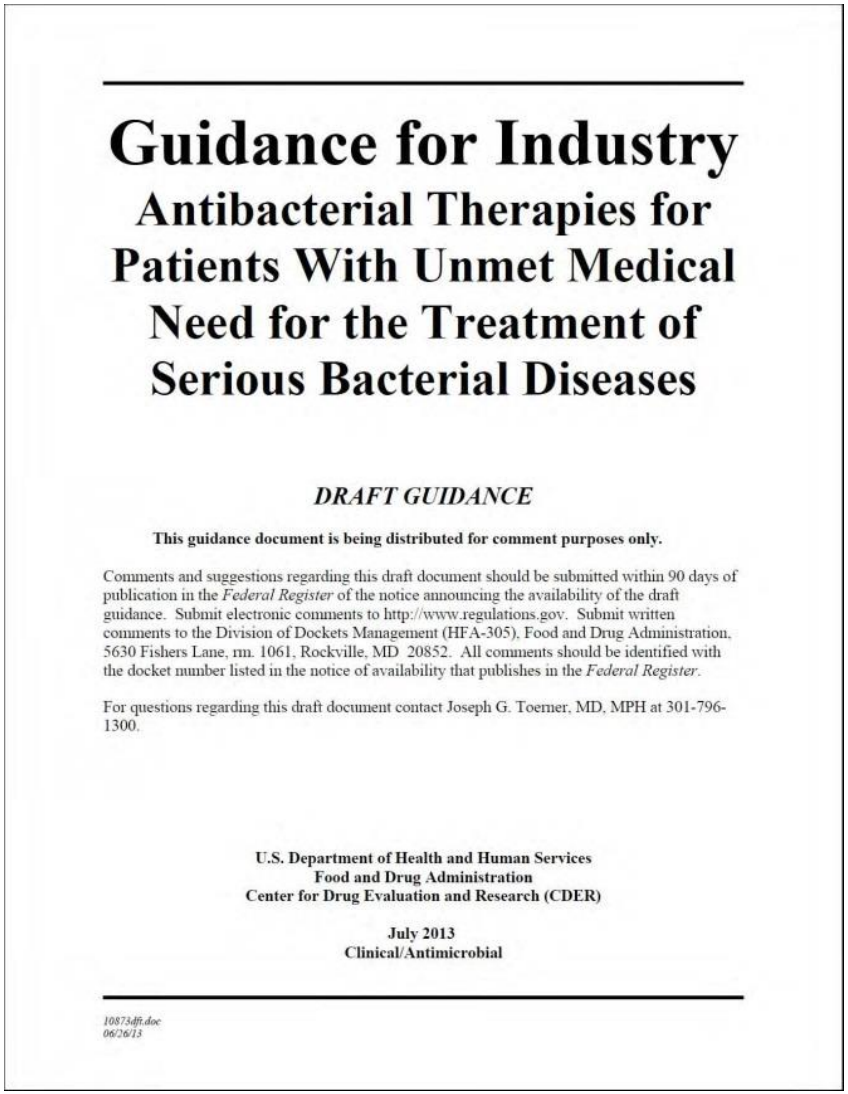
Current Situation

- Resistance continues to create areas of unmet need; patients with few or no appropriate therapeutic options
  - Multi-drug resistant Gram-negative rods
  - Multi-drug resistant *Neisseria gonorrhoeae*
- Need to keep pace with development of new mechanisms of resistance
- Development of a new drug can take 5-10 years
  - Difficult to react in a timely fashion once resistance has occurred
  - Some development programs not successful
  - Ideally have options to choose from in advance of the need

Unmet Need

- Draft guidance issued 2013

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM359184.pdf



Guidance for Industry

Antibacterial Therapies for Patients With Unmet Medical Need for the Treatment of Serious Bacterial Diseases

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.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be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance.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 http://www.regulations.gov. Submit written comments to the Division of Dockets Management (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 Joseph G. Toerner, MD, MPH at 301-796-1300.

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

July 2013
Clinical/Antimicrobial

10873dft.doc
06/26/13

Unmet Need: General Considerations

- Smaller data package; greater uncertainty about risks/benefits
  - One adequate and well-controlled trial with supportive evidence
  - Infections at different body sites can be pooled for certain trial designs
- Greater uncertainty could be acceptable for patient populations with serious disease that do not have other treatment options (21 CFR 312.80, subpart E)
- Healthcare community should be aware of greater uncertainty about risks and benefits in such development programs
- Risks and benefits communicated appropriately in labeling

Unmet Need: Statutory Standards

- Drugs approved on the basis of a streamlined development program must still meet the statutory standards for effectiveness of the FD&C Act
  - Substantial evidence as "evidence consisting of adequate and well-controlled investigations, including clinical investigations,…"
  - Section 115(a) of the Modernization Act: allowed for data from one adequate and well controlled clinical investigation and confirmatory evidence to establish effectiveness
  - 21 CFR 314.126(b): Adequate and well-controlled studies
- Guidance on Providing Clinical Evidence of Effectiveness for Human Drugs and Biological Products, describes FDA's flexibility within these statutory requirements.

Unmet Need: Trial Designs Adequate and Well Controlled

- Noninferiority
- Superiority
  - Active control
  - External controls
  - Add on: Test drug + SOC vs. SOC + Placebo
- Nested noninferiority-superiority

Generating Antibiotic Incentives Now (GAIN)

- Title VIII of the Food and Drug Administration Safety and Innovation Act (FDASIA)
- Enacted on July 9, 2012
- Provides incentives for the development of certain antibacterial and antifungal drug products designated as Qualifying Infectious Disease Products (QIDP)
- QIDP refers to an antibacterial or antifungal human drug that is intended to treat serious or life-threatening infections

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

GAIN - Incentives

- **Additional 5 years marketing exclusivity** granted at the time of approval for products that have been granted a QIDP designation
- **Priority review** for marketing applications for products that have a QIDP designation
- Products that have been granted a QIDP designation are eligible for **fast track** designation
  - Request for fast track should be made when QIDP requested; can only be requested with an active IND

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

Expedited Programs

- Final guidance issued May 2014

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.

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

Expedited Programs

- **Fast Track** (FDAMA 1997): serious condition; potential to address unmet medical need; opportunities for frequent interactions with review team
- **Priority Review** (PDUFA 1992): serious condition; improvement in safety or effectiveness; 6-month
- Breakthrough Therapy (FDASIA 2012): serious condition; prelim clinical evidence indicate potential improvement over existing therapies; actions to expedite the review
- Accelerated Approval

Unmet Need

21 CFR 312.80

"The Food and Drug Administration (FDA) has determined that it is appropriate to exercise the broadest flexibility in applying the statutory standards, while preserving appropriate guarantees for safety and effectiveness. These procedures reflect the recognition that physicians and patients are generally willing to accept greater risks or side effects from drugs that treat life-threatening and severely-debilitating illnesses, than they would accept from drugs that treat less serious illnesses. These procedures also reflect the recognition that the benefits of the drug need to be evaluated in light of the severity of the disease being treated."