Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
April 13, 2017

Location: Tommy Douglas Conference Center, The Ballroom, 10000 New Hampshire Avenue, Silver Spring, Maryland, 20903

Topic: The committee discussed the development of antibacterial drugs that treat a single species of bacteria when the target species infrequently causes infections; examples of such drugs include those that are only active against *Pseudomonas aeruginosa* or *Acinetobacter baumannii*.

These summary minutes for the April 13, 2017 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration were approved on June 5, 2017.

I certify that I attended the April 13, 2017 meeting of the Antimicrobial Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/

Lauren D. Tesh, PharmD, BCPS
Designated Federal Officer, AMDAC

/S/

Lindsey R. Baden, MD
Chairperson, AMDAC

Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
April 13, 2017

The following is the final report of the Antimicrobial Drugs Advisory meeting held on April 13, 2017. A verbatim transcript will be available in approximately six weeks, sent to the Division of Anti-Infective Products and posted on the FDA website at: https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/Anti-InfectiveDrugsAdvisoryCommittee/ucm551361.htm

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The Antimicrobial Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on April 13, 2017, at the Tommy Douglas Conference Center, the Ballroom, 10000 New Hampshire Ave., Silver Spring, MD 20903. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA. The meeting was called to order by Lindsey R. Baden, MD (Chairperson). The conflict of interest statement was read into the record by Lauren D. Tesh, PharmD, BCPS (Designated Federal Officer). There were approximately 85 people in attendance for the meeting. There were four (4) Open Public Hearing speakers.

Issue: The committee discussed the development of antibacterial drugs that treat a single species of bacteria when the target species infrequently causes infections; examples of such drugs include those that are only active against *Pseudomonas aeruginosa* or *Acinetobacter baumannii*.

Attendance:

Antimicrobial Drugs Advisory Committee Members Present (Voting): Ellen M. Andrews, PhD (Consumer Representative); Lindsey R. Baden, MD (Chairperson); Nina M. Clark, MD; Amanda H. Corbett, PharmD, BCPS, FCCP; Demetre C. Daskalakis, MD, MPH; Dean A. Follmann, PhD; Michael D. Green, MD, MPH; Barbara M. Gripshover, MD; Jonathan R. Honegger, MD; Vincent Lo Re, MD, MSCE; Ighovwerha Ofotokun, MD, MSc; Joanna M. Schaenman, MD, PhD; Peter Weina, MD, PhD, FACP, FIDSA

Antimicrobial Drugs Advisory Committee Members Not Present (Voting): None

Antimicrobial Drugs Advisory Committee Members Not Present (Non-Voting): Nicholas A. Kartsonis, MD (Industry Representative)

Temporary Members (Voting): John E. Bennett, MD; Matthew Bidwell Goetz, MD; Joan F. Hilton, DSc, MPH; Debra G. McCall, MBA (Patient Representative); Thomas A. Moore, MD; Yu Shyr, PhD; Melvin P. Weinstein, MD

Acting Industry Representative to the Committee (Non- Voting): Lynn Marks, MD

FDA Participants (Non-Voting): Edward M. Cox, MD, MPH; Sumathi Nambiar, MD, MPH; Yuliya I. Yasinskaya, MD; Peter Kim, MD, MS; Dionne L. Price, PhD; Daniel B. Rubin, PhD

Open Public Hearing Speakers: Stephanie Fox-Rawlings, PhD (National Center for Health Research); Joseph Brodine (National Physicians Alliance); Peter Doshi, PhD; John Rex, MD

The agenda was as follows:

Call to Order and Introduction of Committee	**Lindsey R. Baden, MD** Chairperson, AMDAC
Conflict of Interest Statement	**Lauren D. Tesh, PharmD, BCPS** Designated Federal Officer, AMDAC
FDA Introductory Remarks	**Edward Cox, MD, MPH** Director Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
FDA PRESENTATIONS	
Regulatory Background	**Sumathi Nambiar, MD, MPH** Director Division of Anti-Infective Products (DAIP) Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
March 2017 FDA Public Workshop Summary	**Yuliya Yasinskaya, MD** Medical Team Leader, DAIP Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA
INDUSTRY PRESENTATION	
Challenges with Clinical Trial Design for a Drug Targeting a Single Species of Bacteria: *Acinetobacter baumannii*	**Robin Isaacs, MD** Chief Medical Officer Entasis Therapeutics
FDA PRESENTATION	
Example of a Development Program Targeting *Pseudomonas aeruginosa*	**Peter Kim, MD, MS** Medical Officer, DAIP Office of Antimicrobial Products (OAP) Office of New Drugs (OND), CDER, FDA

BREAK

PRESENTATION BY PROFESSIONAL ORGANIZATION

Developing Anti-infective Drugs for Patients with Unmet Need	**Trish Perl-DeLisle, MD** Chief, Division of Infectious Diseases UT Southwestern Medical Center Infectious Diseases Society of America Board of Directors

Clarifying Questions

LUNCH

OPEN PUBLIC HEARING

BREAK

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the unmet medical need for single species specific products and the risks and benefits of the development proposals presented; please provide any additional recommendations you might have for developing such products.

   Committee Discussion: *The committee agreed that there is an unmet medical need for single species specific products. It was further stated that this unmet need is increasing due to medical comorbidities of patients. The committee commented that studies in humans are complex to conduct due to diagnostic uncertainty at the time of presentation in addition to the use of pre-trial and concomitant antibacterial drugs which further confound the finding of efficacy. The committee did not endorse the use of animal models as the sole source of efficacy data. The committee collectively recommended consideration of the following strategies for developing these products (depending on the case specifics): using a noninferiority clinical trial design, following a mini sentinel model to evaluate safety postmarketing, creating global clinical trials networks, using rapid diagnostics, creating a drug distribution network, imposing postmarketing restrictions, and indicating in the label that such drugs should only be used for salvage treatment. The committee also noted a need to incentivize industry to develop products targeting single bacterial species. Please see the transcript for details of the committee discussion.*

2. **DISCUSSION**: While every effort will be made to perform human clinical trials, performing clinical trials for antibacterial drugs that treat a single species of bacteria when the target species infrequently causes infections will be challenging and data collected may not be interpretable or may be very limited. Should this circumstance arise, it may be useful to consider whether animal models of serious bacterial infections can provide useful information to assess the activity and efficacy of the drug. In such a situation, please discuss the following:

    a. The types of animal models and appropriate endpoints that you think might be useful to assess the efficacy of an investigational agent.

    b. If there is a situation where efficacy is principally demonstrated in animal models of infection and only limited clinical trial data are available in humans, how might such a product be used clinically?

    Committee Discussion: *The committee agreed that clinical trials for products that target a single species of bacteria may have interpretability issues. It was further stated that development programs for antibacterial drugs that target single bacterial species cannot be analogous to that of antibacterial drugs targeting agents of bioterrorism where clinical trials are not feasible. In addition, it was stated that current animal models for P. aeruginosa and A. baumannii do not appear to provide certainty regarding potential applicability of efficacy findings to the human condition. The committee again expressed discomfort in relying on animal models as the sole source of efficacy data. However, robust data from animal models could be highly complementary to limited clinical data. The committee stated that clinical trials in this field although difficult could be conducted when industry, academia, professional societies, and regulators work together. In addition, post approval pathways linking access to the drug to generate additional robust clinical safety and efficacy data could (and should) be established. It was also stated that additional discussions might be needed to define the scope of limited clinical data necessary for approval that is proportional to the nature of the disease and the potential benefit of the product under investigation. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:34 p.m.