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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

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**Food and Drug Administration**

**[Docket No. FDA–2008–N–0225]**

## Antimicrobial Resistance; Public Hearing; Request for Comments

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of public hearing; request for comments.

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**SUMMARY:** The Food and Drug Administration (FDA) is announcing a public hearing on antimicrobial resistance. FDA is seeking general information about the problem of antimicrobial resistance, recommendations as to possible approaches to contain the problem of antimicrobial resistance, responses to specific questions (see section III of this document), and other pertinent information from interested parties. In addition, interested parties may provide views on which serious and life-threatening infectious diseases, such as diseases due to gram-negative bacteria and other diseases due to antimicrobial-resistant bacteria, potentially qualify for available grants and contracts or other development incentives.

**DATES:** The public hearing will be held April 28, 2008, from 8 a.m. to 5 p.m. Submit written or electronic notices of participation by close of business on April 21, 2008. Written or electronic comments will be accepted until May 26, 2008.

**ADDRESSES:** The public hearing will be held at the University System of Maryland Shady Grove Center, 9630 Gudelsky Dr., Rockville, MD 20850.

See **REGISTRATION TO ATTEND AND/OR PARTICIPATE IN THE PUBLIC HEARING** for instructions on how to submit electronic notices of participation.

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Submit written comments to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.regulations.gov*. All comments should be identified with the docket number found in brackets in the heading of this document.

**FOR FURTHER INFORMATION CONTACT:** Nancy Stanisic, Office of Critical Path Programs (HF–18), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–1660, FAX 301–443–9718, *nancy.stanisic@fda.hhs.gov*.

**REGISTRATION TO ATTEND AND/OR PARTICIPATE IN THE PUBLIC HEARING:** To ensure there is sufficient room we ask that you pre-register. If you wish to make an oral presentation during the open public comment period of the hearing, state your intention to present on your registration submission. To register, please send an electronic mail message to *nancy.stansic@fda.hhs.gov* by April 21, 2008. Your e-mail should include the following information:

- Your name,
- Title,
- Business affiliation,
- Address,
- Telephone and fax numbers, and e-mail address.

Please submit a written statement at the time of registration, identifying by number each discussion question you wish to address and the approximate time requested to make your presentation. Organizations should provide this information as well as the names and addresses of all participants. Registered individuals will be notified of the scheduled time for their presentation prior to the hearing. Depending on the number of presentations, FDA may need to

limit the time allotted for presentations. However, the administrative record of the hearing will remain open after the hearing, and written comments may be submitted to the docket as described in section V of this document. Presentations will be limited to the subject matter identified in section III of this document.

FDA will accept walk-in registration at the site, but space is limited. FDA will try to accommodate all persons who wish to make a public comment at the hearing, including those who register at the site. Registration is on a first-come, first-served basis.

Additionally, please notify FDA (see **FOR FURTHER INFORMATION CONTACT**) if you need any special accommodations (such as wheelchair access) at the time of registration.

**SUPPLEMENTARY INFORMATION:**

## I. Background

Antimicrobial drug resistance is a major public health concern and a threat to the effectiveness of existing antimicrobial drugs. Antimicrobial resistant pathogens continue to emerge that are very difficult to treat and that may cause serious or life-threatening diseases. Emerging antimicrobial resistance among many bacteria (e.g., *Pseudomonas* species, *Acinetobacter* species, *Enterococcus* species, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Mycobacterium tuberculosis*) and changes in virulence (e.g., *Clostridium difficile*, group A *Streptococci*, *Escherichia coli* O157:H7, and *Staphylococcus aureus*) are major public health concerns. Timely development of new therapeutic agents is essential and use of existing therapies to treat infections caused by these organisms should be optimized to preserve their utility in treating infections and reduce the rate at which resistance develops.

FDA has been working closely with other Government agencies and organizations to address the issue of antimicrobial resistance. An interagency Task Force began looking at antimicrobial resistance in 1999, and developed and published the *Public Health Action Plan to Combat Antimicrobial Resistance (Action Plan)* (available at *http://www.cdc.gov/drugresistance/actionplan/html/index.htm*).[1] FDA also published a final rule in February 2003 that requires incorporation of information on antimicrobial resistance and prudent use in the labeling of systemic antibacterial drug products for human use (68 FR 6062, February 6, 2003). FDA has held or participated in a number of meetings on antimicrobial resistance, including an Anti-Infective Drugs Products Advisory Committee in March 2003, an Infectious Diseases Society of America/International Society of Anti-Infective Pharmacology/FDA Workshop on Antimicrobial Drug Development in April 2004, and an FDA Science Board Advisory Committee meeting on the Center for Veterinary Medicine's National Antimicrobial Resistance Monitoring System in April 2007.

In September 2007, Congress passed the Food and Drug Administration Amendments Act (FDAAA), which was signed into law by the President on September 27, 2007 (Public Law 110–85). Section 1112 (Orphan Antibiotic Drugs) of FDAAA requires the Commissioner of Food and Drugs (the Commissioner) to convene a public hearing to discuss which serious and life-threatening infectious diseases, such as diseases caused by gram-negative bacteria and other diseases due to antibiotic-resistant bacteria, potentially qualify for available grants and contracts under section 5(a) of the Orphan Drug

[1] (FDA has verified the Web site address, but FDA is not responsible for any subsequent changes to the Web site after this document publishes in the **Federal Register**.)

Act (21 U.S.C. 360ee(a)) or other incentives. For this reason, FDA is holding this public hearing.

Under the Orphan Drug Act (Public Law 97–414), a drug is an orphan drug if it is intended for use in a rare disease or condition. Sponsors of orphan drugs are eligible for certain research and development incentives. During the period that an orphan drug is in development, the sponsor may be awarded grant funding to defray the cost of qualified clinical testing incurred in connection with the development of the drug for a rare disease or condition. A drug that has been designated as an orphan drug by FDA may receive 7 years of marketing exclusivity for the drug for the designated orphan use upon approval. To receive designation as an orphan drug (as defined in section 526 of the Federal Food, Drug, and Cosmetic Act) (21 U.S.C. 360bb)), a sponsor must meet the requirements in 21 CFR 316.20 and 316.21. These requirements include, but are not limited to, documentation of the following:

- The disease or condition for which the drug is intended affects fewer than 200,000 people in the United States (e.g., tuberculosis, malaria, trypanosomiasis).

- If the drug is a vaccine, diagnostic drug, or preventative drug, the persons to whom the drug will be administered in the United States are fewer than 200,000 per year.

- For a drug intended for diseases or conditions affecting 200,000 or more people, or for a vaccine, diagnostic drug, or preventative drug to be administered to 200,000 or more persons per year in the United States, there is no reasonable expectation that costs of research and development of the drug for the indication can be recovered by sales of the drug in the United States.

Antimicrobial drugs that have qualified for orphan drug designation in the past include some indicated for the treatment of tuberculosis, malaria, and trypanosomiasis.

**II. Purpose and Scope of the Hearing**

This hearing is intended to provide the infectious disease community, sponsors, and other interested parties an opportunity to discuss their experience with and concerns about the emerging threat of antimicrobial resistance, possible strategies fostering prudent use to prevent the development of antimicrobial resistance, and the potential for the provisions of the Orphan Drug Act or other incentives to facilitate antimicrobial drug development, including what, if any, conditions might be required to accompany such incentives.

**III. Issues for Discussion**

FDA invites comments from interested parties on the following questions:

1. Please discuss strategies that should be considered to limit the development of antimicrobial resistance, and studies that could be done to assess the utility, safety and effectiveness of those strategies. Possible examples include limiting the approved conditions of use, limiting the duration of therapy, restricting distribution to encourage appropriate use, using shorter courses of therapy with higher doses of antimicrobials, and using directly observed therapy.

2. Please discuss the possible utility and effectiveness of economic incentives in promoting drug development for antimicrobial resistant organisms.

a. What is the potential role of the Orphan Drug Act in providing incentives to facilitate antimicrobial drug development? Please describe the serious and life-threatening infectious diseases for which the Orphan Drug Act

provides viable research and development incentives. Please comment on the potential complexities associated with identifying appropriate orphan populations in the infectious disease context.

b. Are there specific incentives (other than those provided by the Orphan Drug Act) that could facilitate the development of new antimicrobial therapies for serious and life-threatening diseases? Describe those serious and life-threatening infectious diseases, such as diseases due to gram-negative bacteria and other diseases due to antimicrobial-resistant bacteria, which could be considered under an alternative incentive program.

**IV. Notice of Hearing Under 21 CFR Part 15**

The Commissioner is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, accompanied by FDA senior management from the Office of the Commissioner, the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and FDA's Office of Orphan Drugs.

Under § 15.30(f), the hearing is informal, and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation.

Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (part 10 (21 CFR part 10), subpart C)). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b).

To the extent that the conditions for the hearing, as described in this notice, conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in 21 CFR 15.30(h).

**V. Request for Comments**

Regardless of attendance at the public hearing, interested persons may submit written or electronic comments to the Division of Dockets Management (see **ADDRESSES**). Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments should be identified with the docket number found in brackets in the heading of this document. To ensure consideration, submit comments by (see **DATES**). Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA through FDMS only.

**VI. Transcripts**

Please be advised that as soon as a transcript is available, it will be accessible at *http://www.fda.gov/ohrms/dockets/ac/acmenu.htm*. It may be viewed at the Division of Dockets Management (see **ADDRESSES**). A transcript will also be available in either hardcopy or on CD–ROM, after submission of a Freedom of Information request. Written requests are to be sent to Division of Freedom of Information (HFI–35), Office of Management Programs, Food and Drug Administration, 5600 Fishers Lane, rm. 6–30, Rockville, MD 20857.

Dated: 4/9/08

April 9, 2008.

Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

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