

**FOR FURTHER INFORMATION CONTACT:**

Sumati Nambiar, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6232, Silver Spring, MD 20993-0002, 301-796-1300; or Joseph G. Toerner, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6244, Silver Spring, MD 20993-0002, 301-796-1300.

**SUPPLEMENTARY INFORMATION:****I. Background**

FDA is announcing the availability of a draft guidance for industry entitled "Community-Acquired Bacterial Pneumonia: Developing Drugs for Treatment." The purpose of this draft guidance is to assist clinical trial sponsors and investigators in the development of antibacterial drugs for the treatment of CABP. Issues in CABP clinical trials were discussed at a 2008 workshop cosponsored by FDA and professional societies. Recently, there have been additional discussions about clinical trial design and endpoints for CABP at several meetings of the Anti-Infective Drugs Advisory Committee. As a result of these public discussions, the science of clinical trial design and our understanding of endpoints and approaches to clinical development have advanced.

This revised draft guidance supersedes the draft guidance published in March 2009 and informs sponsors of the changes in our recommendations. Although we acknowledge the challenges in conducting clinical trials of investigational antibacterial drugs in CABP, this revised draft guidance incorporates changes intended to attain a greater degree of balance between the practicability of conducting CABP clinical trials and the trial procedures needed for a scientifically sound and interpretable trial. We are specifically requesting input from the public on these changes for consideration before finalizing the guidance. Specifically, the changes from the 2009 draft guidance include:

- A description of two potential primary efficacy endpoints for CABP clinical trials: (1) Improvement in patient symptoms early in the course of therapy for CABP (at day 3 to day 5) and (2) all-cause mortality.
- A justification for a noninferiority margin based on clinical responses observed early in the course of therapy, as well as a justification for all-cause mortality as a primary efficacy endpoint.
- Suggestions for efficacy analyses based on: (1) An overall ITT population

and (2) a microbiological intent-to-treat population consisting of those patients who have a documented bacterial pathogen known to cause CABP.

- An approach for accommodating enrollment of patients who have received prior antibacterial therapy, provided certain constraints are met.

Issuance of this guidance fulfills a portion of the requirements of Title VIII, section 804, of the Food and Drug Administration Safety and Innovation Act (Publ. L. 112-144), which requires FDA to "review and, as appropriate, revise not fewer than 3 guidance documents per year . . . for the conduct of clinical trials with respect to antibacterial and antifungal drugs. . . ."

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

**II. The Paperwork Reduction Act of 1995**

This draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 312 have been approved under OMB control number 0910-0014 and the collections of information in 21 CFR part 314 have been approved under OMB control number 0910-0001.

**III. Comments**

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see **ADDRESSES**). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

**IV. Electronic Access**

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/>

[Guidances/default.htm](http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm) or <http://www.regulations.gov>.

Dated: January 6, 2014.

**Leslie Kux,**

*Assistant Commissioner for Policy.*

[FR Doc. 2014-00255 Filed 1-9-14; 8:45 am]

**BILLING CODE 4160-01-P**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES****Food and Drug Administration**

**[Docket Nos. FDA-1975-N-0355 (Formerly 75N-0185), FDA-1976-N-0272 (Formerly 76N-0056), FDA-1976-N-0344 (Formerly 76N-0057), FDA-1978-N-0701 (Formerly 78N-0070), FDA-1979-N-0224 (Formerly 79N-0169), and FDA-1983-N-0297 (Formerly 83N-0030); DESI 1626, 3265, 12283, and 50213]**

**Drugs for Human Use; Drug Efficacy Study Implementation; Certain Prescription Drugs Offered for Various Indications; Final Resolution of Hearing Requests Under Dockets**

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

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing that all outstanding hearing requests pertaining to Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) have been withdrawn. Shipment in interstate commerce of any of the products identified in these dockets, or any identical, related, or similar (IRS) product to the products in these dockets, that is not the subject of an approved new drug application (NDA) or abbreviated new drug application (ANDA) (other than an over-the-counter (OTC) product that complies with an applicable OTC monograph) is unlawful as of the effective date of this notice.

**DATES:** *Effective Date:* This notice is effective January 10, 2014.

**ADDRESSES:** All communications in response to this notice should be identified with the appropriate docket number and directed to Sakineh Walther, Division of Prescription Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5242, Silver Spring,

MD 20993-0002, *sakineh.walther@fda.hhs.gov*.

**FOR FURTHER INFORMATION CONTACT:**

Sakineh Walther, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5242, Silver Spring, MD 20993-0002, 301-796-3349, *sakineh.walther@fda.hhs.gov*.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In a notice published in the **Federal Register** of July 24, 2012 (77 FR 43337) (the July 24, 2012, notice), FDA described the outstanding hearing requests pertaining to, among others, Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) established under the Agency's Drug Efficacy Study Implementation (DESI) program. In the July 24, 2012, notice, FDA offered an opportunity for companies with outstanding hearing requests under those dockets to withdraw or affirm their outstanding hearing requests.

*A. Docket No. FDA-1975-N-0355 (Formerly 75N-0185) (DESI 3265)*

In 1971, FDA published DESI efficacy findings for single-ingredient anticholinergic drugs for oral or injectable use containing dicyclomine hydrochloride (HCl), among other ingredients (36 FR 11754, June 18, 1971). In a notice published on November 11, 1975 (40 FR 52644), FDA determined that the June 18, 1971, **Federal Register** notice should not have included drugs containing certain specified ingredients, including dicyclomine HCl, because the drugs containing those ingredients were not anticholinergic drugs (40 FR 52644 at 52648). Elsewhere in the **Federal Register** of November 11, 1975 (40 FR 52649), FDA published a notice concluding that dicyclomine HCl products, among other products covered by the notice, were less than effective and offering an opportunity for hearing regarding these drugs.

On June 22, 1984, in response to the submission of data, FDA published a followup notice regarding single entity dicyclomine HCl products (49 FR 25681). In that notice, FDA concluded that such products were effective for the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, and mucous colitis) and

established conditions for their marketing and labeling (49 FR 25681 at 25683 and 25684). The Agency also found, however, that the products were lacking substantial evidence of effectiveness for use in the treatment of acute enterocolitis or infant colic (49 FR 25681 at 25684) and offered an opportunity for hearing.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Merrell-National Laboratories, 110 Amity Rd., Cincinnati, OH 45215, regarding Bentyt Capsules (NDA 7-409), Bentyt Injection (NDA 8-370), Bentyt Syrup (NDA 7-961), and Dactil Tablets (NDA 8-907). FDA believes Sanofi-Aventis U.S. to be the successor-in-interest to Merrell-National Laboratories, but received no response to its attempt to contact Sanofi-Aventis U.S. regarding this hearing request in September 2011. In the July 24, 2012, notice, FDA provided the company an opportunity to affirm or withdraw its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

*B. Docket Nos. FDA-1976-N-0272 (Formerly 76N-0056), FDA-1976-N-0344 (Formerly 76N-0057), and FDA-1978-N-0701 (Formerly 78N-0070) (DESI 1626)*

In 1972, FDA classified certain combination drug products containing a xanthine derivative as lacking substantial evidence of effectiveness for some labeled indications and possibly effective for other labeled indications (37 FR 14895, July 26, 1972). As described in a **Federal Register** notice of February 29, 1984 (49 FR 7454), FDA subsequently handled these products in three groups:

Group 1: Combinations containing 2 grains or less of a xanthine derivative, ephedrine, and 8 milligrams (mg) or less of phenobarbital (Docket No. FDA-1976-N-0344 (formerly 76N-0057));

Group 2: Combinations containing more than 2 grains of xanthine derivative, more than 8 mg of phenobarbital, and/or an ingredient not considered as part of the OTC drug review (Docket No. FDA-1976-N-0272 (formerly 76N-0056)); and

Group 3: Combinations containing theophylline, ephedrine, and hydroxyzine HCl (Docket No. FDA-1978-N-0701 (formerly 78N-0070)).

With respect to the products in Group 2, a notice of opportunity for hearing was published on April 9, 1976 (41 FR 15051). No hearing was requested, and approval of applications for products covered by Docket No. FDA-1976-N-

0272 (formerly 76N-0056) (DESI 1626) were withdrawn by notice in the **Federal Register** published October 7, 1977 (42 FR 54620).

With respect to the products in Group 3, FDA granted a hearing in response to requests (49 FR 36443, September 17, 1984). The hearing requests were subsequently withdrawn, and approval of applications for products covered by Docket No. FDA-1078-N-0701 (formerly 78N-0070) (DESI 1626) were withdrawn by notice in the **Federal Register** published July 8, 1998 (63 FR 36923).

With respect to the products in Group 1, in 1976, FDA granted temporary permission for the products to remain on the market because similar products had been marketed OTC in the past and were then undergoing review in the Over-the-Counter Drug Study (41 FR 15053, April 9, 1976). In 1984, FDA amended the April 1976 notice to include its analysis of new information regarding combination products containing a xanthine derivative (49 FR 7454, February 29, 1984). Based on its analysis of the new information, FDA concluded that there is a lack of substantial evidence: (1) That each ingredient contributes to the claimed effect of such combination drug products and (2) that the dosage of each component is such that the combinations are safe and effective for a significant patient population (49 FR 7454). Therefore, FDA proposed in the 1984 notice to withdraw approval of the applications for combination products containing a xanthine derivative and offered an opportunity for hearing regarding its proposal.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under Docket No. FDA-1976-N-0344 (formerly 76N-0057) filed by William P. Poythress & Co, Inc., 16 N. 22nd St., P.O. Box 26946, Richmond, VA 23261, regarding an unidentified product containing a xanthine derivative, ephedrine, and 8 mg or less of phenobarbital. FDA was unable to find current contact information for William P. Poythress & Co, Inc. In the July 24, 2012, notice FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

*C. Docket No. FDA-1979-N-0224 (Formerly 79N-0169) (DESI 12283)*

In 1979, FDA announced its DESI conclusions regarding the effectiveness of chlorthalidone for the treatment of hypertension and certain types of edema (44 FR 54124, September 18, 1979).

Specifically, FDA determined that there was substantial evidence to support the effectiveness of the 25- and 50-mg strengths for use in hypertension and edema, but that there was no longer justification for the 100-mg dosage form of chlorthalidone because of safety concerns at that dosage level (44 FR 54124 at 54126). In the 1979 notice, FDA proposed to withdraw approval of the 100-mg strength and offered an opportunity for hearing regarding its proposal.

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Generics International Division of Apotex, Inc., 2400 North Commerce Pkwy., Suite 400, Weston, FL 33326, regarding chlorthalidone. In the July 24, 2012, notice, FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

*D. Docket No. FDA-1983-N-0297 (Formerly 83N-0030) (DESI 50213)*

Under Docket No. FDA-1983-N-0297 (formerly 83N-0030), FDA evaluated the evidence of effectiveness for certain fixed-combination drugs containing antibiotics and sulfonamides and determined that these products lacked substantial evidence of effectiveness (34 FR 6008, April 2, 1969). In the April 1969 **Federal Register** notice, FDA proposed to revoke provisions for certification of these products, and offered interested persons 30 days to submit data concerning the proposal. Data submitted in response to the April 1969 notice did not provide substantial evidence of effectiveness, so FDA amended the antibiotic regulations on June 30, 1970, by revoking provisions for the certification of these drugs (35 FR 10587, June 30, 1970). The order was to become effective in 40 days and allowed 30 days for interested persons to file objections and request a hearing. The time for responding to the June 1970 order was subsequently extended until August 17, 1970 (35 FR 12653, August 8, 1970).

In response to the June 1970 order, Pfizer Inc. submitted data regarding its affected product, Urobiotic 250 Capsules, and requested a hearing. Despite the filing of timely objections, the amendments were inadvertently not stayed, and succeeding codifications of the antibiotic regulations did not explicitly provide for certification of Urobiotic 250 Capsules. However, FDA permitted Pfizer to continue distribution of its product pending resolution of the firm's hearing request. In July 2010,

Pfizer voluntarily withdrew its application for Urobiotic (see 75 FR 42455, July 21, 2010).

At the time of the July 24, 2012, notice, there was one outstanding hearing request under this docket filed by Pfizer, Inc., 235 East 42nd St., New York, NY 10017, regarding Urobiotic. As noted in the previous paragraph, the product itself was withdrawn, but FDA attempted to contact the company to verify that it no longer wished to pursue its hearing request. The company did not respond, and in the July 24, 2012, notice, FDA provided this company an opportunity to withdraw or affirm its hearing request. Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.

## II. Resolution of Hearing Requests Pertaining to Dockets Subject to This Notice

The time period for responding to the July 24, 2012, notice has elapsed, and no companies with outstanding hearing requests pertaining to the dockets listed in this document responded to the notice. Because no outstanding hearing requests relating to these dockets were affirmed in response to the July 24, 2012, notice (or in response to FDA's previous attempts to contact companies with outstanding hearing requests), all of the outstanding hearing requests pertaining to Docket Nos. FDA-1975-N-0355 (formerly 75N-0185) (DESI 3265); FDA-1976-N-0272 (formerly 76N-0056), FDA-1976-N-0344 (formerly 76N-0057), and FDA-1978-N-0701 (formerly 78N-0070) (DESI 1626); FDA-1979-N-0224 (formerly 79N-0169) (DESI 12283); and FDA-1983-N-0297 (formerly 83N-0030) (DESI 50213) are deemed to be withdrawn.

Effective as of the date of this notice, it is unlawful to introduce into interstate commerce any of the products identified in any of the dockets included in this notice, or any IRS product to any product identified in these dockets, that is not the subject of an approved NDA or ANDA. Any person who wishes to determine whether a specific product is covered by this notice should write to the Center for Drug Evaluation and Research (see **ADDRESSES**).

## III. Discontinued Products

Some firms may have previously discontinued manufacturing or distributing products covered by this notice without removing them from the listing of their products under section 510(j) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C.

360(j)). Other firms may discontinue manufacturing or distributing listed products in response to this notice. Firms that wish to notify the Agency of product discontinuation should send a letter identifying the discontinued product(s), including the National Drug Code number(s), and stating that the manufacturing and/or distribution of the product(s) has (have) been discontinued. The letter should be sent electronically to Sakineh Walther (see **ADDRESSES**).

Firms should also electronically update the listing of their products under section 510(j) of the FD&C Act to reflect discontinuation of products covered by this notice. Firms should be aware that, after the effective date of this notice, FDA intends to take enforcement action without further notice against any firm that manufactures or ships in interstate commerce any unapproved product covered by this notice.

Dated: January 6, 2014.

**Leslie Kux,**

*Assistant Commissioner for Policy.*

[FR Doc. 2014-00256 Filed 1-9-14; 8:45 am]

**BILLING CODE 4160-01-P**

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2013-N-1658]

### Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks in Drug Regulatory Decision-Making; Public Workshop; Request for Comments

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

**ACTION:** Notice of Public Workshop; request for public comments.

**SUMMARY:** The Food and Drug Administration (FDA or the Agency) is announcing the following workshop convened by the Institute of Medicine (IOM): "Characterizing and Communicating Uncertainty in the Assessment of Benefits and Risks in Drug Regulatory Decision-Making." The purpose of the workshop is twofold: To explore potential approaches to addressing and communicating uncertainty and to identify key considerations on developing, evaluating, and incorporating potential approaches for addressing uncertainty into the assessment of benefits and risks in the human drug review process. The format of the meeting consists of a series of presentations on topics related to uncertainty in the assessment of benefits