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 Requests that were not affirmed within 30 days of that notice were to be deemed by FDA to be withdrawn.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

and risks, followed by a discussion on those topics with invited panelists and audience members. This workshop satisfies an FDA commitment that is part of the fifth authorization of the Prescription Drug User Fee Act (PDUFA V).

DATES: The public workshop will be held on February 12, 2014, from 8:30 a.m. to 4:30 p.m. and February 13, 2014, from 8:30 a.m. to 3:30 p.m. Registration to attend the public workshop must be received by January 31, 2014. See the **SUPPLEMENTARY INFORMATION** section for information on how to register for the workshop. Submit either electronic or written comments by March 14, 2014.

ADDRESSES: The public workshop will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., Building 31 Conference Center, Rm. 1503A, Silver Spring, MD 20993–0002. Entrance for public workshop attendees (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to *http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.*

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. Identify all comments with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Sara Eggers, Food and Drug Administration, Center for Drug Evaluation and Research, 10903 New Hampshire Ave., Bldg. 51, Rm. 1166, Silver Spring, MD 20993–0002, 301–796–4904, FAX: 301–847–8443, email: *sara.eggers@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

On July 9, 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144). Title I of FDASIA reauthorizes PDUFA and provides FDA with the user fee resources necessary to maintain an efficient review process for human drug and biological products. The reauthorization of PDUFA includes performance goals and procedures for the Agency that represents FDA's commitments during fiscal years 2013–2017. These commitments are fully described in the document entitled ''PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017'' (PDUFA Goals Letter), available on FDA's Web site at *http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf.*

Section X of the PDUFA Goals Letter, entitled ''Enhancing Benefit-Risk Assessment in Regulatory Decision-Making,'' includes development of a plan to further develop and implement a structured approach to benefit-risk assessment in the human drug review process. As part of this enhancement, FDA committed to holding two public workshops on benefit-risk considerations from the regulator's perspective that will begin by the first quarter of fiscal year 2014. The public workshop announced in this notice will fulfill the first of the two workshop commitments.

As part of its commitment, FDA has published the ''Structured Approach to Benefit-Risk Assessment in Drug Regulatory Decision-Making: Draft PDUFA V Implementation Plan,'' available on FDA's Web site at *http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM329758.pdf.* In this plan, FDA identified as an area of further development the exploration of structured approaches to evaluate and communicate the uncertainty in the assessment of benefits and risks. FDA's human drug regulatory decisions are informed by an extensive body of evidence on the safety and efficacy of a drug product. In many cases, this evidence is subject to uncertainty arising from many sources. One example is the uncertainty in the degree to which premarket clinical trial data translates to the postmarket setting after the drug is approved and used in a much wider patient population. Another example is uncertainty about a potential safety signal that emerges in the postmarket setting, where the basis for the finding comes from multiple evidence sources of varying levels of rigor. Drawing conclusions in the face of uncertainty can be a complex and challenging task. Furthermore, being explicit about the impact of uncertainty on decision-making is an important part of communicating regulatory decisions.

II. Purpose and Scope of the Workshop

This 2-day public workshop is being convened by IOM. The public workshop will explore more systematic and structured approaches to evaluate and communicate: (1) The sources of uncertainty in the assessment of benefits and risks and (2) their implications on human drug regulatory decisions. Specifically, the workshop will explore potential analytical and communication approaches to addressing and communicating uncertainty and 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. This public workshop will consider the entire drug development life cycle, including premarket drug review and postmarket safety surveillance. The format of the meeting consists of a series of presentations on topics related to uncertainty in the assessment of benefits and risks, followed by a discussion on those topics with invited panelists and audience members.

III. Attendance and Registration

FDA's Conference Center at the White Oak location is a Federal facility with security procedures and limited seating. Persons interested in attending the public workshop must register online by January 31, 2014. To register for the public workshop, please visit FDA's workshop Web site at *http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm378861.htm.* Early registration is recommended. Registration is free and will be on a first-come, first-served basis. However, the number of participants from each organization may be limited based on space limitations. Registrants will receive confirmation once they have been accepted. Onsite registration on the day of the workshop will be based on space availability. If you need special accommodations because of disability, please contact Sara Eggers (see **FOR FURTHER INFORMATION CONTACT**) at least 7 days before the workshop. More information will be made available on FDA's workshop Web site at least 5 days before the workshop date.

A live Webcast of this workshop will be viewable on FDA's workshop Web site at *http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm378861.htm* on the day of the workshop. A video recording of the workshop will be available on FDA's workshop Web site approximately 1 week following the workshop. IOM will independently prepare a summary of the workshop, and the summary will be available on FDA's workshop Web site approximately 10 months following the workshop.

IV. Comments

Regardless of attendance at the public workshop, interested persons may submit either electronic comments 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. To ensure consideration, submit comments by March 14, 2014. 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.*

Dated: January 6, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014–00258 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–1485]

Unapproved and Misbranded Oral and Injectable Drugs Labeled for Prescription Use Containing Codeine Sulfate, Codeine Phosphate, or Dihydrocodeine Bitartrate; Enforcement Action Dates

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing its intention to take enforcement action against unapproved and misbranded oral and injectable drug products labeled for prescription use and containing codeine sulfate, codeine phosphate, or dihydrocodeine bitartrate, and against persons who manufacture or cause the manufacture or distribution of such products in interstate commerce. Prescription drug products containing these ingredients pose serious risks, including the risk of addiction, and some unapproved drug products may lack warnings or other information required in the labeling of approved drug products that is important for safe use. These unapproved drug products compete with approved drug products and thus pose a direct challenge to the drug approval system. This document covers the following unapproved drug products labeled for prescription use: Single-ingredient codeine sulfate oral tablets and solutions, single-ingredient codeine phosphate injection products, fixed-dose combination products containing codeine phosphate, and fixed-dose combination products containing dihydrocodeine bitartrate. A new drug containing codeine sulfate, codeine phosphate, or dihydrocodeine bitartrate requires an approved new drug application (NDA) or abbreviated new drug application (ANDA) to be legally marketed.

DATES: This document is effective January 10, 2014. For information about enforcement dates, see the **SUPPLEMENTARY INFORMATION**, section IV.

ADDRESSES: All communications in response to this document should be identified with Docket No. FDA–2013–N–1485 and directed to the appropriate office listed in this **ADDRESSES** section:

Applications under section 505(b) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 355(b)): Division of Anesthesia, Analgesia and Addiction Products (for products with analgesic indications) or Division of Pulmonary, Allergy, and Rheumatology Products (for products with antitussive indications), Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Silver Spring, MD 20993–0002.

Applications under section 505(j) of the FD&C Act: Office of Generic Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855.

All other communications: Astrid Lopez-Goldberg, Office of Unapproved Drugs and Labeling Compliance, Division of Prescription Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5185, Silver Spring, MD 20993–0002.

FOR FURTHER INFORMATION CONTACT: Astrid Lopez-Goldberg, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5185, Silver Spring, MD 20993–0002, 301–796–3485, *Astrid.LopezGoldberg@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

Codeine is an opioid used primarily as an analgesic to relieve pain or as an antitussive to treat coughs. Codeine sulfate and codeine phosphate are different salts of codeine, generally also for analgesic or antitussive use. Dihydrocodeine bitartrate is a chemical derivative of codeine and an opioid pain reliever that produces effects similar to those of codeine.

Side effects are similar among all opioids and include light-headedness, dizziness, drowsiness, headache, fatigue, sedation, sweating, nausea, vomiting, constipation, itching, and skin reactions. Serious adverse effects are respiratory depression, resulting in a slow breathing rate, and decreased blood pressure. Multiple active ingredients (including acetaminophen, aspirin, butalbital, caffeine, carisoprodol, promethazine, or phenylephrine) may be marketed in combination with codeine phosphate or dihydrocodeine bitartrate. Some of these fixed-dose combination products include more than one sedating component.

Single-ingredient products containing codeine, such as codeine sulfate oral tablets and solutions, and codeine phosphate injection products, are schedule II narcotics (§ 1308.12 (21 CFR 1308.12)) under the Controlled Substances Act (21 U.S.C. 801 et seq.). Single-ingredient prescription codeine sulfate oral tablets and a single-ingredient prescription codeine sulfate oral solution are approved for the relief of mild to moderately severe pain. On October 13, 2009, the Agency issued four warning letters to companies manufacturing and/or marketing unapproved prescription codeine sulfate oral tablets.[1] However, FDA is aware of at least one unapproved prescription codeine sulfate oral tablet that is still listed with FDA's Drug Registration and Listing System. Although FDA is unaware of any unapproved single-ingredient codeine phosphate injection products on the market at this time, such products were on the market as recently as 2010.

Fixed dose combination products containing codeine phosphate are placed on different schedules under the Controlled Substances Act depending on their use:

- Fixed-dose combination products containing codeine, which are generally used as analgesics in pediatric and adult patients, are typically schedule III or schedule V drugs under the Controlled Substances Act depending on the amount of codeine contained in the drug (§§ 1308.13 and 1308.15 (21 CFR 1308.13 and 1308.15)).[2] FDA is aware of a safety concern with an unapproved fixed-dose combination product containing codeine phosphate and acetaminophen that is labeled for analgesic use. We note that this product does not have the Boxed Warning for liver toxicity that would be required if this were an approved product (76 FR 2691, January 14, 2011).

[1] Available at *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm238675.htm#codeine_sulfate.*

[2] We note that at dosages exceeding the maximum identified in § 1308.13 these fixed dose combination drug products would be Schedule II.