Dated: May 22, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E7–10271 Filed 5–25–07; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N–0193]

Timed-Release Drug Products Containing Guaifenesin; Enforcement Action Dates

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its intention to take enforcement action against unapproved drug products in timed-release dosage forms containing guaifenesin and persons who cause the manufacture or interstate shipment of such products. Hundreds of unapproved drug products in timed-release form containing guaifenesin, alone or in combination with other ingredients, are marketed to relieve the symptoms associated with cough, cold, and similar conditions. Such drug products require approved applications because they are not generally recognized as safe and effective for these uses. One firm has obtained approved applications to market timed-release products containing guaifenesin. Other firms who wish to market a drug product in timed-release form containing guaifenesin must obtain FDA approval of a new drug application (NDA) or an abbreviated new drug application (ANDA).

DATES: This notice is effective May 29, 2007.

For marketed, unapproved drug products in timed-release form containing guaifenesin that have a National Drug Code (NDC) number that is listed with FDA under section 510 of the act (21 U.S.C. 360) on the effective date of this notice (i.e., ''currently marketed products''), the agency intends to exercise its enforcement discretion to permit products properly marketed with those NDC numbers a brief period of continued marketing after May 29, 2007 as follows. FDA does not intend to initiate enforcement actions against firms that are manufacturing such currently marketed products unless those firms are still manufacturing the products on or after August 27, 2007. Further, FDA does not intend to initiate enforcement actions related to the shipment in interstate commerce of currently marketed products made by such firms unless they are still being shipped on or afterNovember 26, 2007. Unapproved drug products in timed-release form containing guaifenesin that are not currently marketed products on the date of this notice must, as of the date of this notice, have approved applications prior to their shipment in interstate commerce. Submission of an application does not excuse timely compliance with this notice.

ADDRESSES: All communications in response to this notice should be identified with Docket No. 2007N–0193 and directed to the appropriate office listed as follows:

Regarding applications under section 505(b) of the act (21 U.S.C. 355(b)): Division of Pulmonary and Allergy Products, 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.

Regarding applications under section 505(j) of the act: Office of Generic Drugs, Center for Drug Evaluation and Research (HFD–600), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

All other communications: Sakineh Walther, Division of New Drugs and Labeling Compliance, Center for Drug Evaluation and Research (HFD–310), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Sakineh Walther, Center for Drug Evaluation and Research (HFD–310), Food and Drug Administration, 11919 Rockville Pike, Rockville, MD 20852, 301–827–8964, e-mail: *sakineh.walther@FDA.HHS.GOV*.

SUPPLEMENTARY INFORMATION:

I. Background

Guaifenesin is an expectorant that has been marketed for decades. Thousands of products intended to relieve symptoms associated with cough, colds, allergies and similar conditions are marketed containing guaifenesin, alone or in combination with other active ingredients, such as antitussives (for instance, dextromethorphan or hydrocodone), nasal decongestants (for instance, pseudoephedrine or phenylephrine), and analgesics (for instance, acetaminophen). These products are marketed both over-the-counter (OTC) and by prescription, and in immediate- and timed-release dosage forms.

Guaifenesin in immediate-release form was reviewed in the OTC drug review and is covered by the OTC monograph in part 341 (21 CFR part 341), ''Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use.'' OTC products that comply with this monograph may be marketed without approval.

The OTC monograph system does not include timed-release drug products, a dosage form that is designed to release the active ingredients over a prolonged period of time. Since 1959, the agency has stated that all products in timed-release dosage forms also described as, for example, sustained release, extended release, controlled release, or long-acting—are new drugs requiring approved applications (24 FR 3756, May 9, 1959). Agency review of individual applications is needed to ensure that the finished product releases its active ingredients at a rate that is both safe, without ''dumping'' of the dose, and effective, sustaining the intended effect over the entire period during which the therapeutic benefit is claimed. Firms submitting applications are required to establish appropriate release specifications supported by clinical evidence, along with data showing that the finished product as manufactured by the firm releases its active ingredient according to these specifications. The agency's determination that all products in timed-release form are new drugs requiring approved applications is codified in § 310.502(a)(14) (21 CFR 310.502(a)(14)). The regulation applies to all products in this dosage form containing guaifenesin, alone or in combination with other active ingredients.

II. Current Status of Timed-Release Drug Products Containing Guaifenesin

One firm has obtained approved applications for products in timed-release dosage forms containing guaifenesin. Adams Respiratory Therapeutics, formerly known as Adams Laboratories, Inc. (Adams), submitted an NDA for single-ingredient guaifenesin tablets in timed-release form (NDA 021–282), which was approved by FDA on July 12, 2002. These products are sold OTC under the trade names of MUCINEX (600 milligrams (mg)) and HUMIBID (1,200 mg), with labeling for uses consistent with expectorant products marketed under an OTC monograph (§ 341.78(b)). Specifically, MUCINEX and HUMIBID are intended to help ''loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus, and make coughs more productive.'' On October 11, 2002, the agency notified firms marketing single-

ingredient, timed-release products containing guaifenesin without approved applications that their products were unapproved new drugs marketed in violation of section 505 of the act and that they must cease marketing them. The agency did not at that time address products in timed-release form that combined guaifenesin with other active ingredients.

Subsequently, Adams submitted applications for OTC timed-release combination products containing guaifenesin and dextromethorphan, an antitussive (NDA 21–620), and guaifenesin and pseudoephedrine, a decongestant (NDA 21–585). The agency approved these applications on April 29, 2004, and June 22, 2004, respectively. These products are marketed OTC under the trade names MUCINEX–DM and MUCINEX–D, respectively. Both products are labeled for use as expectorants. In addition, MUCINEX–DM is labeled for antitussive uses as permitted under the OTC monographs (§ 341.74(b)) and MUCINEX–D is labeled for nasal decongestant uses as permitted under the OTC monographs (§ 341.80(b)).

Hundreds of products in timed-release form containing guaifenesin in combination with other active ingredients such as antitussives and decongestants are marketed without approved applications for relief of various symptoms associated with cough, cold, allergy, and similar conditions. Because no applications have been filed and reviewed by the agency for these products, the safety and effectiveness of the products cannot be ensured. For instance, the agency does not know if the firms that market them have established appropriate specifications for release of the active ingredients; whether the products are properly formulated and manufactured so as to release their ingredients at a rate that is both safe and effective; and whether each active ingredient in the combination makes a contribution to the claimed effect, as required by 21 CFR 300.50.

Many of these unapproved drug products in timed-release form containing guaifenesin are marketed, labeled, and dispensed as prescription products. Section 503(b)(1) of the act (21 U.S.C. 353(b)(1)) establishes the definition of a prescription drug. Drug products that do not meet the definition of a prescription drug but are labeled for prescription use are considered misbranded under section 503(b)(4) of the act. Some firms choose to market drugs as prescription, even though those drugs do not meet the prescription drug definition, either because of the availability of reimbursement by insurers or because of familiarity with the distribution channels for prescription drugs. This is contrary to the act.

III. Legal Status

A. Timed-Release Products Containing Guaifenesin Are New Drugs Requiring Approved Applications

Under § 310.502(a)(14), drug products in timed-release dosage forms containing guaifenesin are not generally recognized as safe and effective for any use because of the need for agency review of individual applications to ensure the safe and effective release of active ingredients. Therefore, a drug product in timed-release form containing guaifenesin, alone or in combination with other drugs, is regarded as a new drug, as defined in section 201(p) of the act (21 U.S.C. 321(p)), and is subject to the requirements of section 505 of the act. As set forth in this notice, approval of an NDA under section 505(b) of the act (including section 505(b)(2)) and 21 CFR 314.50 or an ANDA under section 505(j) of the act and 21 CFR 314.94 is required as a condition for manufacturing or marketing all such products. After the dates identified in this notice (see **DATES**), FDA intends to take enforcement action, as described in this notice, against unapproved drug products in timed-release form containing guaifenesin and persons who cause the manufacture or interstate shipment of such products. Submission of an application does not excuse timely compliance with this notice.

The Adams timed-release products containing 1,200 mg of guaifenesin marketed under NDA 021–282, NDA 21–620, and NDA 21–585, as described in section I of this notice, have been designated as reference listed drug products. The review and approval of any applications for timed-release drug products containing guaifenesin will be subject to the patent rights of the current NDA holder.

B. Notice of Enforcement Action

Although not required to do so by the Administrative Procedure Act, the act, or any rules issued under its authority, or for any other legal reason, FDA is providing this notice to firms that are marketing timed-release drug products containing guaifenesin without an approved application that the agency intends to take enforcement action against such products and those who cause them to be manufactured or shipped in interstate commerce. Consistent with the priorities identified in the agency's guidance entitled ''Marketed Unapproved Drugs—Compliance Policy Guide'' (the Marketed Unapproved Drugs CPG), the agency is taking action at this time against these products because the agency has approved applications to market timed-release drug products containing guaifenesin, alone and in combination with other active ingredients, for relief of cough, cold, and allergy symptoms; thus, the continued marketing of unapproved timed-release guaifenesin products is a direct challenge to the drug approval process. Manufacturing or shipping such unapproved products may result in seizure, injunction, or other judicial proceeding. Consistent with policies described in the Marketed Unapproved Drugs CPG, the agency does not expect to issue a warning letter or any other further warning to firms marketing unapproved timed-release drug products containing guaifenesin prior to taking enforcement action. The agency also reminds firms that, as stated in the Marketed Unapproved Drugs CPG, any unapproved drug marketed without a required approved drug application is subject to agency enforcement action at any time. The issuance of this notice does not in any way obligate the agency to issue similar notices or any notice in the future regarding other marketed unapproved drugs.[1]

As described in the Marketed Unapproved Drugs CPG, the agency may, in its discretion, exercise enforcement discretion and identify a period of time during which the agency does not intend to initiate an enforcement action against a currently marketed unapproved drug on the grounds that it lacks an approved application under section 505 of the act, to preserve access to medically necessary drugs, or ease disruption to affected parties, for instance. The agency notes that there are numerous marketed products that have approved applications or comply with an applicable OTC drug monograph and that are used to treat conditions for which products in timed-release form containing guaifenesin are commonly used. Therefore, the agency intends to implement this notice as follows.

This notice is effective May 29, 2007. Unapproved timed-release drug products containing guaifenesin, alone

[1] The agency's general approach in dealing with these products in an orderly manner is spelled out in the Marketed Unapproved Drugs CPG. However, the CPG provides notice that any product that is being marketed illegally, and the persons responsible for causing the illegal marketing of the product, are subject to FDA enforcement action at any time.

or in combination with other active ingredients, that are not currently marketed products on the effective date of this notice must, as of this date, have approved applications prior to their shipment in interstate commerce. However, for unapproved timed-release guaifenesin products that are currently marketed as of the date of this notice (i.e., timed-release guaifenesin products that are not approved but have an NDC number that is listed with the agency on the effective date of this notice), the agency intends to exercise its enforcement discretion to permit the products marketed with those NDC numbers a period of continued marketing after May 29, 2007 as follows. FDA does not intend to initiate enforcement actions against firms that are manufacturing currently marketed products unless those firms are still manufacturing the products on or after August 27, 2007. Further, FDA does not intend to initiate enforcement actions related to the shipment in interstate commerce of currently marketed products made by such firms unless they are still being shipped on or after November 26, 2007.[2] The agency, however, does not intend to exercise its enforcement discretion as outlined in this paragraph if: (1) A manufacturer or distributor of an unapproved product covered by this notice is violating other provisions of the act or (2) it appears that a firm, in response to this notice, increases its manufacture or interstate shipment of drug products covered by this notice above its usual volume during these periods.

Drug manufacturers and distributors should be aware that the agency is exercising its enforcement discretion as described previously only in regard to timed-release drug products containing guaifenesin that are marketed under an NDC number listed with the agency on the effective date of this notice. Such unapproved drug products that are not currently marketed and listed with the agency on the effective date of this notice must, as of the effective date of this notice, have approved applications prior to their shipment in interstate commerce. Moreover, submission of an application does not excuse timely compliance with this notice.

[2] If a firm continues to manufacture or market a product covered by this notice after the applicable enforcement date has passed, to preserve limited agency resources, FDA may take enforcement action relating to all of the firm's unapproved drugs that require applications at the same time (see, e.g., *United States* v. *Sage Pharmaceuticals*, 210 F.3d 475, 479–480 (5th Cir. 2000) (permitting the agency to combine all violations of the act in one proceeding, rather than taking action against a firm with multiple violations of the act in ''piecemeal fashion'')).

C. Discontinued Products

Some firms may have previously discontinued the manufacturing or distribution of products covered by this notice without removing them from the listing of their products under section 510(j) of the act. Other firms may discontinue manufacturing or marketing listed products in response to this notice. Firms that wish to notify the agency of product discontinuation should send a letter, signed by the firm's chief executive officer, fully identifying the discontinued product(s), including its NDC number(s), and stating that the product(s) has (have) been discontinued and will not be marketed again without FDA approval, to Sakineh Walther (see **ADDRESSES**). Firms should also update the listing of their products under section 510(j) of the act to reflect discontinuation of unapproved timed-release products containing guaifenesin. FDA plans to rely on its existing records, the results of a subsequent inspection, or other available information when it initiates enforcement action.

D. Reformulated Products

In addition to discontinuing the manufacturing of products covered by this notice, FDA cautions firms against reformulating their products into guaifenesin-free unapproved new drugs that are marketed under the same name or substantially the same name (including a new name that contains the old name). In the Marketed Unapproved Drugs CPG, FDA states that it intends to give higher priority to enforcement actions involving unapproved drugs that are reformulated to evade an FDA enforcement action. In addition, reformulated products marketed under a name previously identified with a different active ingredient or combination of active ingredients have the potential to confuse health care practitioners and harm patients. Depending on the circumstances, these products may be considered misbranded under section 502(a) or (i) of the act (21 U.S.C. 352(a) and (i)).

This notice is issued under the act (sections 502 and 505) and under authority delegated to the Deputy Commissioner for Policy under section 1410.10 of the FDA Staff Manual Guide.

Dated: May 15, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E7–10266 Filed 5–25–07; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N–0204]

Joint Meeting of the Gastrointestinal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming meeting of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

Name of Committees: Gastrointestinal Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee.

General Function of the Committees: To provide advice and recommendations to the agency on FDA's regulatory issues.

Date and Time: The meeting will be held on July 31, 2007, from 8 a.m. to 5 p.m.

Addresses: Electronic comments should be submitted to *http://www.fda.gov/dockets/ecomments*. Select ''2007— Efficacy and Safety of TYSABRI (natalizumab) for Patients With Moderately to Severely Active Crohn's Disease'' and follow the prompts to submit your statement. Written comments should be submitted to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments received will be posted without change, including any personal information provided. Comments received on or before July 24, 2007, will be provided to the committee before the meeting.

Location: Holiday Inn, The Ballrooms, Two Montgomery Village Ave., Gaithersburg, MD.

Contact Person: Victoria Ferretti-Aceto, Center for Drug Evaluation and Research (HFD–21), Food and Drug Administration, 5600 Fishers Lane (for express delivery, 5630 Fishers Lane, rm. 1093), Rockville, MD 20857, 301–827–7001, FAX: 301–827–6776, e-mail: *Victoria.FerrettiAceto@fda.hhs.gov*, or FDA Advisory Committee Information Line, 1–800–741–8138 (301–443–0572) in the Washington, DC area), codes 301–451–2538 and 301–451–2535. Please call the Information Line for up-to-date information on this meeting. A notice in the **Federal Register** about last minute modifications that impact a previously