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## **Unapproved Prescription Cough, Cold, and Allergy Drug Products : Recent US Food and Drug Administration Regulatory Action on Unapproved Cough, Cold, and Allergy Medications**

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## Unapproved Prescription Cough, Cold, and Allergy Drug Products

### Recent US Food and Drug Administration Regulatory Action on Unapproved Cough, Cold, and Allergy Medications

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The US Food and Drug Administration (FDA) drug approval and over-the-counter drug monograph processes play an essential role in ensuring that all drugs are both safe and effective for their intended uses. Manufacturers of drugs that lack required approval have not provided the FDA with evidence demonstrating that their products are safe and effective. Some of these prescription drugs have been marketed for many years and have remained on the market despite changes to the Federal Food, Drug, and Cosmetic Act, which requires approval for safety and efficacy purposes. Many health-care providers may be unaware that unapproved drugs exist because the product labels of these drugs do not disclose that they lack FDA approval. The FDA recently took action against unapproved prescription oral cough, cold, and allergy drug products because of concerns about the potential risks of these products, particularly some extended-release formulations that have not been reviewed for quality. There is a potential for medication errors because product names and labeling have not been reviewed for potential confusion, with some products inappropriately labeled for use in children aged  $\leq 2$  years. FDA-approved prescription drugs or drugs appropriately marketed as over the counter remain available for treatment of cough, cold, and allergy symptoms. Such products are of known efficacy, safety, identity, quality, and purity. Removing unapproved drugs from the marketplace and encouraging manufacturers of unapproved products to seek FDA review and approval is a top priority for the FDA. Since the initiation of the Unapproved Drugs Initiative in 2006, the FDA has removed  $\sim 1,500$  unapproved products from the market and has worked with firms to bring other unapproved drugs into the approval process. The FDA remains committed to its mission of ensuring that safe and effective drugs are available to American consumers. *CHEST 2011; 140(2):295–300*

**Abbreviations:** ACCP = American College of Chest Physicians; ANDA = abbreviated new drug application; DESI = Drug Efficacy Study Implementation; FDA = US Food and Drug Administration; FD&C = Federal Food, Drug, and Cosmetic; GRAS/E = generally recognized as safe and effective; IRS = identical, related, or similar; NAS/NRC = National Academy of Sciences/National Research Council; NDA = new drug application; NDC = National Drug Code; OTC = over the counter

The new drug approval and over-the-counter (OTC) drug monograph processes play an essential role in ensuring that all drugs are both safe and effective for their intended uses. Drugs that have approved new drug applications (NDAs), abbreviated new drug applications (ANDAs), or active ingredients and labeling that are in accordance with an OTC drug monograph may be marketed legally in the United States (Table 1<sup>1,2</sup>). Manufacturers of drugs that lack required approval, including those that are not marketed in accordance with an OTC drug monograph, have not

provided the US Food and Drug Administration (FDA) with evidence demonstrating that their products are safe and effective. Many health-care providers may be unaware that unapproved drugs exist

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because drug product labels do not document FDA approval.

Under the Federal Food, Drug, and Cosmetic (FD&C) Act, all “new drugs”<sup>3</sup> are required to obtain

approval under section 505<sup>4</sup> prior to marketing. Most drugs are considered new drugs under the FD&C Act, but a drug may be excluded from being deemed a new drug (and, therefore, not required to obtain approval under section 505) if it is “generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective [GRAS/E] for use under the conditions prescribed, recommended, or suggested in the labeling thereof.” The GRAS/E standard is outlined in Table 2.<sup>3,5</sup> The FDA believes that it is not likely that any currently marketed prescription drug is GRAS/E<sup>6</sup> because the standard is very high. Even though there may be excellent clinical studies of various prescription drug products reported in the literature, it is highly unlikely that these reports have the same quality and quantity of scientific data as that in an NDA.

#### FD&C ACT AND DRUG APPROVAL

The Federal Food and Drugs Act of 1906 brought drug regulation under federal law. That act prohibited the sale of adulterated or misbranded drugs but did not require that drugs be approved by the FDA. The act has since been amended a number of times, often in response to tragedies.<sup>7,8</sup> The 1938 amendment to the FD&C Act required that the FDA review and approve new drugs for safety but not effectiveness before they could be sold legally in interstate commerce. The FD&C Act made it the sponsor's burden to show the FDA that the drug was safe through the submission of an NDA. Between 1938 and 1962, the FDA considered drugs that were identical, related, or similar (IRS) to an approved drug to be “covered” by that approval, and allowed those IRS drugs to be marketed without independent approval.

In 1962, Congress amended the FD&C Act to require that new drugs be proven effective for their labeled indications as well as safe. This amendment also required the FDA to conduct a retrospective evaluation of effectiveness for all drugs approved as safe between 1938 and 1962. The FDA contracted

with the National Academy of Sciences/National Research Council (NAS/NRC) to make an initial evaluation of the effectiveness of the products that had been approved only for safety between 1938 and 1962. The FDA's administrative implementation of the NAS/NRC reports in the 1970s was called the Drug Efficacy Study Implementation (DESI). DESI covered the ~3,400 products specifically reviewed by the NAS/NRC as well as the even larger number of IRS products that entered the market without FDA approval. All drugs covered by the DESI review are considered new drugs under the FD&C Act. Therefore, drug products with NDAs approved before 1962 for safety require approved supplements to their original applications if found effective under DESI; IRS drug products require an approved NDA or ANDA, as appropriate.

#### COMMON MISCONCEPTIONS SURROUNDING UNAPPROVED DRUGS

Health-care providers should be alert to the fact that an advertisement in a reputable medical journal, inclusion in pharmaceutical references, a National Drug Code (NDC) number, or even availability on the pharmacy shelf does not guarantee that a product has received FDA approval or otherwise conforms to the OTC monograph process. Additionally, because many unapproved drugs have been marketed for many years, are without brand names, or are marketed as lower-cost alternatives to approved brand-name products, there may be an inaccurate perception among prescribers and consumers that these unapproved drugs are approved generic drugs when in fact they are not. Although the term “generic” is commonly used to refer to the chemical name of a drug, generic drugs are evaluated and approved by the FDA and generally are required, among other things, to be bioequivalent to a brand-name reference product. Additionally, the generic drug manufacturing, packaging, and testing must meet the same quality standards as those of brand-name drugs.

#### CONCERNS WITH UNAPPROVED NEW DRUGS

Marketed unapproved prescription drugs are a significant public health concern because they have not been comprehensively evaluated by the FDA and may not meet modern standards for safety, effectiveness, manufacturing quality, and labeling. For example, the FDA review process determines whether there is substantial evidence to support the clinical efficacy of the product for the intended use, dose, duration, and patient population.<sup>5</sup>

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**Table 1—Regulation and Approval of Drug Products Legally Marketed in the United States**

|                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| NDA                 | NDAs are the formal submissions of data that sponsors send the FDA when they are seeking approval to market a new drug in the United States. Some NDAs are for new molecular entities; however, NDAs also can be for an active substance previously sold in a different form. NDAs include not only detailed clinical data but also detailed data supporting the identity, strength, quality, and purity of active and inactive ingredients; manufacturing processes; toxicology; and clinical pharmacology of a drug product. Reviews of many NDAs are available to the public at the FDA Web site <a href="http://Drugs@FDA">Drugs@FDA</a> . <sup>1</sup> |
| ANDA                | Applications for generic versions of previously approved drugs are ANDAs. Generic versions of previously approved drugs are not required to repeat the extensive clinical trials used in the development of the original, brand-name drugs. For many products such as tablets and capsules, generics must show bioequivalence to the brand-name reference-listed drug. This means that the generic version must deliver the same amount of active ingredient into a patient's bloodstream over the same time period as the brand-name reference-listed drug.                                                                                                |
| OTC monograph drugs | Products marketed under the specifications of the OTC drug monographs <sup>2</sup> are not subject to FDA review and approval before marketing. OTC drug monographs are federal regulations that specify active pharmaceutical ingredients, doses, formulations, uses, and labeling that are acceptable for marketing as nonprescription drug products. The monographs are developed on the basis of scientific review and finalized through public comment and rulemaking processes.                                                                                                                                                                       |

ANDA = abbreviated new drug application; FDA = US Food and Drug Administration; NDA = new drug application; OTC = over the counter.

Without reviewing applications for unapproved products, the FDA has no way to assess the scientific support, if any, for the statements made in labeling. Its review of an applicant's labeling ensures that health-care professionals and patients have the information necessary to understand a drug product's risks and its safe and effective use. The FDA is interested in minimizing potential safety issues caused by product name confusion. Product names, as part of product labeling, also are reviewed by the FDA. Look-alike and sound-alike similarities between product names are a common cause of medication errors and adverse events.

The FDA has significant concerns regarding the manufacturing processes for unapproved new drugs and changes in the formulations of these products, especially as more ingredients are sourced globally. When new drugs are marketed without FDA approval, the FDA does not have an opportunity to determine whether the manufacturing process can reliably produce drug products of expected identity, strength, quality, and purity. For example, in 1983, a company began marketing a new formulation of a high-potency IV vitamin E without FDA approval. The product was intended to prevent blindness in premature babies. Inactive ingredients in the product were responsible for causing kidney and liver failure and resulted in adverse reactions in about 100 premature babies, 40 of whom died. The product was recalled and removed from the market in early 1984.<sup>9</sup>

Extended-release products are of a particular safety concern because many contain total amounts of active ingredients that could pose safety risks if the same amount of active ingredient were contained in an immediate-release dosage form. Without prior review of applications for these products, there is no assurance that the firms that market these products have established appropriate specifications for release of the active ingredients or that the products are properly formulated and manufactured to actually release their active ingredients to an extent and at a rate that is

both safe and effective. Since 1959, the FDA has considered all extended-release dosage forms as new drugs and has required these products to have approved NDAs/ANDAs.<sup>10</sup>

#### FDA UNAPPROVED DRUGS INITIATIVE

Launched in 2006, the FDA Unapproved Drugs Initiative efficiently and rationally brings all such drugs into the approval process while also serving official notice that any illegally marketed product is subject to FDA enforcement action at any time.<sup>6</sup> The FDA uses a risk-based enforcement program to concentrate its resources on those products that pose the highest threat to public health and without imposing undue burdens on consumers or unnecessarily disrupting the market (including considering whether the product is medically necessary and, if so, the ability of legally marketed products to meet the needs of patients taking the drug). Areas of focus for enforcement include drugs that pose potential safety risks, lack evidence of effectiveness, promulgate health fraud, present direct challenges to the new drug approval and OTC drug monograph systems, are unapproved new drugs that also violate the FD&C Act in other ways, or are reformulated to evade an FDA enforcement action.

Over the past 5 years the FDA has taken 17 class actions, ordering the market removal of ~1,500 drugs from ~400 firms. It also has undertaken a number of injunction and product seizure actions against non-compliant firms. Examples of FDA enforcement actions on unapproved marketed drugs are found in Table 3.

#### 2011 FDA ACTION AGAINST UNAPPROVED COUGH, COLD, AND ALLERGY PRODUCTS

On March 3, 2011, the FDA issued a *Federal Register* notice announcing an enforcement action against companies that manufacture, distribute, or market

certain unapproved oral products labeled for prescription use.<sup>11</sup> Companies that manufacture and sell unapproved cough, cold, and allergy products listed with the FDA were directed to cease both manufacturing within 90 days and shipping within 180 days of March 3, 2011, whereas companies that were not listed with the FDA must halt manufacturing and shipping immediately.

The oral products subject to the action are labeled for the relief of symptoms relating to cold, cough, or allergy and include antihistamines, antitussives, expectorants, and nasal decongestants.<sup>12</sup> They include single-ingredient, multiple-ingredient combinations, extended-release, tannate-containing, and certain immediate-release products. All of the products subject to the FDA action are labeled for prescription<sup>13</sup> use and considered new drugs and either are not considered GRAS/E and do not have approved NDAs/ANDAs or are misbranded and therefore do not bear “adequate directions for use.”<sup>14-16</sup> None of the products was subject to ongoing DESI proceedings.

All of the extended-release products require an approved application to be marketed legally, as noted earlier. The FDA reviewed the publically available scientific literature on the tannate products and determined that none of them are GRAS/E. The tannate products are considered new drugs and are considered misbranded unless they have approved NDAs/ANDAs.

The remaining products subject to FDA action are immediate-release products. A number of the immediate-release products conform to the final cough and cold OTC monograph except for the fact that they are labeled for prescription use only and thus are considered misbranded.<sup>17</sup> These products could be legally marketed as OTC and not be considered new drugs if they were to be relabeled in conformance with the cough and cold OTC monograph. The majority of the immediate-release products contain ingredients included in the cough and cold OTC monograph but are labeled for prescription use and have indications, dosing regimens, or both that are inconsistent with that monograph. The FDA has reviewed both the labeling and the publicly available scientific literature for studies of >300 such products. In no case did the FDA find literature sufficient to support a determination that any of these products was GRAS/E for relief of symptoms of cold, cough, or allergy. Therefore, these products are considered to be both new drugs and misbranded because they fail to bear adequate directions for use.<sup>18</sup>

#### RISKS ASSOCIATED WITH UNAPPROVED COUGH, COLD, AND ALLERGY PRODUCTS OFFERED FOR PRESCRIPTION USE ONLY

The FDA has identified numerous risks associated with the use of unapproved cough, cold, and allergy

**Table 2—Criteria That Must Be Met in Order to Conclude That a Drug Product Is GRAS/E<sup>3</sup>**

1. The particular drug product must have been subjected to adequate and well-controlled clinical investigations that establish the product as safe and effective.
2. Those investigations must have been published in the scientific literature available to qualified experts.
3. Experts must generally agree, based on those published studies, that the product is safe and effective for its intended uses. At a minimum, the general acceptance of a product as GRAS/E must be supported by the same quality and quantity of scientific and clinical data necessary to support the approval of an NDA.<sup>5</sup>

GRAS/E = generally recognized as safe and effective. See Table 1 legend for expansion of other abbreviation.

products covered by the March 3, 2011, action. The products are antihistamines, decongestants, antitussives inappropriately labeled for use in young children and infants; are marketed as extended release; may release active ingredients too slowly, too quickly, or inconsistently; are irrational combinations of active ingredients, such as more than one type of antihistamine; and have potentially confusing or similar sound-alike names.

The pediatric labeling for these unapproved products is a particular concern because some of the unapproved products are labeled and marketed for use in children as young as age 1 month. In 2008, the FDA issued a public health advisory recommending that OTC cough and cold products not be used for infants and children aged <2 years because serious and potentially life-threatening side effects could occur.<sup>19</sup> Many of the unapproved prescription cough, cold, and allergy drugs subject to this enforcement action contain the same ingredients as the OTC cough and cold products discussed in the public health advisory and are labeled for children as young as age 6 months. The safety concerns discussed in the 2008 public health advisory apply to these unapproved prescription drugs as well. The American College of Chest Physicians (ACCP) and the American Academy of Pediatrics have recommended that cough suppressants and other OTC cough medicines should not be used in children with cough, particularly in young children because they may experience significant morbidity and mortality.<sup>20-22</sup>

A number of manufacturing and potential safety issues are relevant to the extended-release and tannate products. Their active ingredients may be released too slowly, too quickly, or inconsistently. FDA laboratory analyses and inspections have found numerous quality issues. These include serious good manufacturing procedure and pharmaceutical deficiencies where pharmaceutical performance varied between products containing the same active ingredient.

Some of the unapproved products have contained more than one antihistamine, raising the concern that

they may be associated with the potential for additive sedative effects of the combination. The FDA has also received reports of name confusion associated with unapproved prescription products covered by the action that could lead to the incorrect drug being provided to a patient.

### ACCP TREATMENT GUIDELINES

The FDA's March 3, 2011, enforcement action has a direct impact on the treatment recommendations made in the 2006 ACCP guideline "Cough and the Common Cold." The guideline states that (1) OTC cough medications are not recommended for cough in children; (2) central cough suppressants have limited efficacy for symptomatic relief and are not recommended; and (3) OTC cold medications or nonsedating antihistamines, except for older antihistamine/decongestant combinations, are not recommended.<sup>23</sup> The guideline recommends that patients with acute cough, postnasal drip, and throat clearing associated with the common cold may be treated with a first-generation antihistamine/decongestant preparation, such as brompheniramine and sustained-release pseudoephedrine.

As a result of the FDA action, extended-release brompheniramine/pseudoephedrine or immediate- or extended-release dexbrompheniramine/pseudoephedrine products will not be available until an application for such products is approved or until a manufacturer brings an OTC monograph-compliant product to the market. Although the lack of availability of extended-release brompheniramine and dexbrompheniramine products may be inconvenient, treatment options remain available (Table 4). An alternative treatment approach would be to use an immediate-release, fixed-combination brompheniramine/pseudoephedrine or brompheniramine/phenylephrine product. Other alternatives include immediate-release chlorphe-

**Table 4—Cough and the Common Cold: Available Treatment Options Consistent With ACCP Guidelines**

|                          |                                                                                                                                                                                                                                                                                                                   |
|--------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Brompheniramine maleate  | <ul style="list-style-type: none"><li>• Immediate-release brompheniramine maleate/pseudoephedrine HCl combination products</li><li>• Immediate-release brompheniramine maleate/phenylephrine HCl combination products</li></ul>                                                                                   |
| Chlorpheniramine maleate | <ul style="list-style-type: none"><li>• Immediate-release chlorpheniramine maleate single-ingredient products</li><li>• Immediate-release chlorpheniramine maleate/pseudoephedrine HCl combination products</li><li>• Immediate-release chlorpheniramine maleate/phenylephrine HCl combination products</li></ul> |
| Pseudoephedrine HCl      | <ul style="list-style-type: none"><li>• Immediate-release pseudoephedrine HCl single-ingredient products</li><li>• Extended-release pseudoephedrine HCl single-ingredient products</li></ul>                                                                                                                      |

ACCP = American College of Chest Physicians; HCl = hydrochloride.

niramine alone; immediate-release chlorpheniramine combined with an immediate- or extended-release pseudoephedrine product; or an immediate-release, fixed-combination chlorpheniramine/pseudoephedrine or chlorpheniramine/phenylephrine product. Because market availability is in a constant state of flux, practitioners should check with their pharmacist regarding local availability of these products.

The FDA has encouraged the manufacturers of these products to work with it to bring products into the approval process so that health-care professionals can be assured that the products they prescribe are of proven efficacy, safety, quality, and purity. The FDA encourages health-care providers to confirm the approval status of prescription medications and that they use official compendia, such as the FDA Orange Book<sup>24</sup> and NDC Directory.<sup>25</sup> Orange Book search results include a column labeled "Appl No." FDA-approved prescription products will have an associated NDA or ANDA number in this column. NDC Directory search results will state, "No matching records found," if a prescription product is not approved. If health-care providers have had a patient experience a serious adverse event with an unapproved product, we encourage the submission of that information to the MedWatch Program.<sup>26</sup> Because many unapproved drugs will remain on the market for the foreseeable future, when selecting drug therapy, the FDA recommends that health-care professionals carefully consider the medical condition being treated, the patient's previous response to a drug, and the availability of FDA-approved alternatives for treatment.

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**Table 3—Examples of FDA Unapproved Drugs Initiative Enforcement Actions**

- Carbinoxamine, an antihistamine associated with 21 infant deaths
- Balanced salt solution (ophthalmic), associated with reports of permanent loss of vision due to product contamination or other product defects
- Ergotamine due to inadequate labeling that did not include warnings regarding the potential for serious, possibly fatal drug interactions
- Sublingual nitroglycerin tablets associated with significant deficiencies in efficacy and quality
- Morphine sulfate oral solution 20 mg/mL associated with fatal medication errors

Additional enforcement actions are listed at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsonUnapprovedDrugs/ucm238675.htm>.

medications. He holds shares in both Cephalon and Merck. These relationships are not related to the topic of this article. Drs Lee and McMeekin have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

**Other contributions:** This article reflects the views of the authors and should not be construed to represent FDA views or policies.

## REFERENCES

1. Drugs@FDA. US Food and Drug Administration Web site. <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>. Accessed April 11, 2011.
2. OTC human drugs that are generally recognized as safe and effective and not misbranded. 21 CFR §§330-358 (2010).
3. Federal Food, Drug, and Cosmetic Act, Sect 201(p), Chap II—Definitions, 21 USC §321 (2011).
4. Federal Food, Drug, and Cosmetic Act, Sect 505, New Drugs, 21 USC §355 (2011).
5. Adequate and well-controlled studies. 21 CFR §314.126 (2010).
6. US Department of Health and Human Services; Food and Drug Administration; Center for Drug Evaluation and Research. Guidance for FDA staff and industry marketed unapproved drugs—compliance policy guide: Sec. 440.100 marketed new drugs without approved NDAs or ANDAs. US Food and Drug Administration Web site. <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM070290.pdf>. June 2006. Accessed April 11, 2011.
7. Secretary of Agriculture. Deaths due to elixir of sulfanilamide-Massengill. *JAMA*. 1937;109(24):1985-1988.
8. Taussig HB. Thalidomide and phocomelia. *Pediatrics*. 1962; 30(4):654-659.
9. Arrowsmith JB, Faich GA, Tomita DK, Kuritsky JN, Rosa FW. Morbidity and mortality among low birth weight infants exposed to an intravenous vitamin E product, E-Ferol. *Pediatrics*. 1989;83(2):244-249.
10. Certain drugs accorded new drug status through rulemaking procedures. 21 CFR §310.502(a)(14) (2010).
11. Drugs for human use; unapproved and misbranded oral drugs labeled for prescription use and offered for relief of symptoms of cold, cough, or allergy; enforcement action dates. *Fed Regist*. 2011;76(42):11794-11798. Codified at 21 CFR § 310.502.
12. US Food and Drug Administration. Unapproved prescription cough, cold, and allergy products. US Food and Drug Administration Web site. <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/EnforcementActivitiesbyFDA/SelectedEnforcementActionsOnUnapprovedDrugs/ucm245106.htm>. Published April 1, 2011. Accessed April 11, 2011.
13. Federal Food, Drug, and Cosmetic Act, Sec 503(b)(1)(A), Exemptions and Consideration for Certain Drugs, Devices, and Biological Products, Chap V—Drugs and Devices, 21 USC §353 (2011).
14. Prescription drugs for human use. 21 CFR §201.100(c)(2).
15. Adequate directions for use. 21 CFR §201.5 (2010).
16. Federal Food, Drug, and Cosmetic Act, Sec 503(b)(4)(B), Exemptions and Consideration for Certain Drugs, Devices, and Biological Products, Chap V—Drugs and Devices, 21 USC §353 (2011).
17. Cold, cough, allergy, bronchodilator and asthmatic drug products for over-the-counter human use. 21 CFR §341 (2010).
18. Federal Food, Drug, and Cosmetic Act, Sec 502(f)(1), Misbranded Drugs and Devices, Chap V—Drugs and Devices, 21 USC §352 (2011).
19. US Food and Drug Administration. Public health advisory: FDA recommends that over-the-counter (OTC) cough and cold products not be used for infants and children under 2 years of age. US Food and Drug Administration Web site. <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/PublicHealthAdvisories/ucm051137.htm>. Published February 23, 2011. Accessed April 11, 2011.
20. Chang AB, Glomb WB. Guidelines for evaluating chronic cough in pediatrics: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(suppl 1):260S-283S.
21. Testimony of David Bromberg, MD, FAAP, on behalf of the American Academy of Pediatrics before the Joint Meeting of the Food and Drug Administration Nonprescription Drugs Advisory Committee and Pediatric Advisory Committee, Silver Spring, Maryland, October 19, 2007. US Food and Drug Administration Web site. <http://www.fda.gov/ohrms/dockets/ac/07/transcripts/2007-4323t2-Part3.pdf>. Accessed April 11, 2011.
22. American Academy of Pediatrics, Committee on Drugs. Use of codeine- and dextromethorphan-containing cough remedies in children. *Pediatrics*. 1997;99(6):918-920.
23. Pratter MR. Cough and the common cold: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(suppl 1): 72S-74S.
24. US Food and Drug Administration. Orange book: approved drug products with therapeutic equivalence evaluations. US Food and Drug Administration Web site. <http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>. Updated December 21, 2010. Accessed April 30, 2011.
25. US Food and Drug Administration. National drug code directory. US Food and Drug Administration Web site. <http://www.accessdata.fda.gov/scripts/cder/ndc-old/default.cfm>. Updated June 1, 2011. Accessed June 1, 2011.
26. US Food and Drug Administration. MedWatch online voluntary reporting form (3500). US Food and Drug Administration Web site. <https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm>. Published April 1, 2011. Accessed April 11, 2011.

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