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December 8, 2005

VIA HAND DELIVERY

Food and Drug Administration
Dockets Management Branch
5630 Fishers Lane, Room 1061
Rockville, MD 20852

**Re: Docket No. 1976N-0052G
Cough, Cold, Allergy, Bronchodilator, and Antiasthmatic Drug Products for
Over-the-Counter Human Use; Proposed Amendment of the Tentative Final
Monograph for Combination Products;**

**Comments Opposing FDA's Proposed Elimination of Ephedrine/Guaifenesin
OTC Combination Drug Products for Treatment of Mild Asthma (70 Fed.
Reg. 40232, July 13, 2005); and**

**Request for Stay of FDA Action Regarding the Proposed Amendment to the
Monograph**

Dear Sir or Madam:

We are writing to you on behalf of our client, the American Council on Regulatory Compliance (the "ACRC"), a group of small businesses that manufacture, distribute and sell over-the-counter ("OTC") drug products including oral bronchodilator/expectorant combinations containing ephedrine salts and guaifenesin for use in the symptomatic treatment of mild asthma.

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PSA 1

The Food and Drug Administration (“FDA”) published two notices in the Federal Register regarding Cough, Cold, Allergy, Bronchodilator, and Antiasthmatic Drug Products for OTC Human Use. One notice proposed retaining OTC status for oral ephedrine salts as Category I (generally recognized as safe and effective for OTC use) bronchodilator single-ingredient products for the treatment of patients with mild asthma. 70 Fed. Reg. 40237, July 13, 2005. The second notice proposed to amend the OTC monograph to reclassify combinations containing an oral bronchodilator (ephedrine or its salts) and an expectorant as Category II (not generally recognized as safe and effective for OTC use.) 70 Fed. Reg. 40232, July 13, 2005.

The ACRC strongly agrees with the FDA’s conclusions with respect to single-entity ephedrine products. For the reasons detailed below, however, the ACRC equally strongly opposes FDA’s proposed reclassification of oral bronchodilator/expectorant products, and requests that FDA stay final action on that proposal pending consideration of additional data recently submitted to the rulemaking docket, and, if necessary, additional data to be developed by the ACRC.

I. Single-Ingredient Ephedrine Products Are Not Readily Available OTC and Therefore Cannot Meet Patients’ Needs in the Treatment of Mild Asthma

The ACRC agrees with FDA’s proposal retaining OTC status for oral ephedrine salts as Category I (generally recognized as safe and effective for OTC use) bronchodilator single-ingredient products for the treatment of patients with mild asthma. Unfortunately, there are only

a very limited number of oral, single ingredient ephedrine products listed in FDA's National Drug Code Directory (three solid oral ephedrine products are listed), and due to severe legal restrictions intended to prevent the products' accessibility for use in illegal methamphetamine production, even these products, to the best of the member's of the ACRC knowledge, are only limitedly available in the commercial marketplace. Indeed, as of November 5, 2005, only two retail outlets in the entire nation were registered with the U.S. Drug Enforcement Administration ("DEA") as required to sell single-ingredient ephedrine products without a prescription. The practical effects of DEA and state restrictions on the sale of ephedrine-containing drug products make single-ingredient OTC ephedrine products essentially unavailable to the general public. Thus, it is ACRC's position that oral, single ingredient ephedrine products are not a viable option and do not meet the needs of patients who suffer from mild asthma who seek to use an OTC product for periodic, symptomatic relief.

II. Oral Bronchodilator/Expectorant Products Containing Guaifenesin Provide Safe, Effective, Rational, and Needed Symptomatic Treatment for Mild Asthma Sufferers

The ACRC respectfully disagrees with FDA's conclusion that an oral bronchodilator in combination with an expectorant is not a rational combination for the treatment of mild asthma. Combination products containing a bronchodilator and expectorant have been on the market for many years and have provided safe and effective symptomatic relief for the symptoms of mild asthma. To date, patients suffering from mild asthma have had wide access to these products to

provide relief, when necessary, from mild asthma symptoms. If these products are reclassified to Category II, many patients will not have access to an OTC product to treat their mild asthma and as a result they may, for example: (a) forgo treatment because there is no affordable OTC product available; (b) forgo treatment because they are unable to afford the cost of a physician visit and a prescription; and/or (c) seek medical care at an emergency room or other health care facility, thereby increasing the cost of medical care and unnecessarily burdening already-overstrained public health care services. It is the ACRC's position that combination oral bronchodilators/expectorant products are safe and effective and play a key role in the treatment of patients who suffer from mild asthma and who desire and get benefit from the OTC products that are currently available in the commercial marketplace.

A. Scientific Data Support the Rationale Including Expectorant Therapy in the Treatment of Mild Asthma

There is a clear scientific rationale for including expectorant therapy in the treatment of mild asthma. As recognized in the proposed reclassification notice, mucus secretion is among the multiple factors that contribute to inflammation and airway obstruction in chronic asthma. Comments submitted by Bayer HealthCare provide evidence that guaifenesin provides significant clinical benefits for patients with mild asthma when used either alone or in combination with a bronchodilator. Moreover, comments submitted to the FDA docket by Wyeth Consumer Healthcare identify multiple recent and ongoing biomechanical studies supported by the National Heart, Lung, and Blood Institute ("NHLBI") demonstrating the

occurrence of mucus-related morphological changes in mild asthma, as well as multiple studies demonstrating a clinical correlation between mucus hypersecretion and asthma symptoms. Both sets of comments provide data supporting the scientific rationale for including an expectorant in combination with a bronchodilator for use in the treatment of mild asthma. *See* Docket No. 1976N-0052G, comments of Bayer HealthCare Consumer Care Division (Nov. 2, 2005) and comments of Wyeth Consumer Healthcare (Nov. 7, 2005).

B. The Marketing History Supports the Safety of Guaifenesin and Ephedrine Combination Drug Products and Benefits of OTC Access to a Product for the Treatment of Mild Asthma

Guaifenesin/ephedrine combination drug products are clearly safe for use in treating mild asthma, as evidenced by their long use and wide acceptance by mild asthma sufferers, as well as the extensive body of scientific data and clinical experience supporting their use in a wide range of single-ingredient and combination products for multiple OTC indications. FDA's speculation in the Federal Register notice that guaifenesin could potentially contribute to harmful mucus plugs is not supported by scientific or clinical evidence.

C. Guaifenesin/Ephedrine Combination Products Offer Significant Additional Benefits to Patients Experiencing Mild Asthma

Guaifenesin/ephedrine combination products offer important benefits to patients compared to the cost and inconvenience of buying and using two separate single-ingredient products. Moreover, as stated above, the ACRC does not believe that access to a single-ingredient ephedrine product is not a practical option for patients suffering from mild asthma symptoms. In particular, the ACRC believes that Drug Enforcement Administration (“DEA”) restrictions on OTC access to single-ingredient ephedrine products create far more than a “minor inconvenience.” Single ingredient ephedrine products are not widely available, if available at all. FDA’s assertion that single ingredient products offer a viable alternative is simply not the case. Asthma is a serious and rapidly growing public health problem that disproportionately affects lower-income families, African Americans, and Hispanic Americans. See U.S. Environmental Protection Agency, Asthma Facts (May 2005). As a practical matter, the added cost and difficulty of consulting a doctor and/or locating and obtaining a single-ingredient ephedrine product available “behind the counter” at a DEA-compliant outlet may effectively deter many such patients who now use and benefit from ephedrine/guaifenesin combination products as a result.

III. Request that FDA Stay Finalization of the Proposed Reclassification

For the reasons stated above, the ACRC requests that FDA: (1) stay finalization of the proposed reclassification; (2) duly consider comments on the clinical evidence and analyses submitted by Bayer HealthCare Consumer Care Division on November 2, 2005 and Wyeth Consumer Healthcare on November 7, 2005 with respect to the medical rationale for combination therapy; and (3) republish in the Federal Register, for further notice and comment, revised conclusions with respect to ephedrine/guaifenesin combination products based on the Bayer and Wyeth data as well as any other relevant data submitted to the rulemaking docket.

In the event that, upon further evaluation, FDA still believes that such a reclassification is warranted, the ACRC respectfully requests that FDA stay finalization of the proposed reclassification until the ACRC has the opportunity to meet with FDA staff, discuss the clinical data to further support rationale of the combination and the design and timetable for carrying out and completing such additional studies, if any, which may be deemed necessary by FDA to support the use of ephedrine/guaifenesin combination products in patients suffering from mild asthma.

VI. Conclusion

The ACRC believes that the existing record as supplemented by recent comments by Bayer Healthcare Consumer Care Division and Wyeth Consumer Healthcare is more than

adequate to support OTC status for ephedrine/guaifenesin combination products. There is a long OTC marketing history of combination products containing a bronchodilator and an expectorant providing safe and effective symptomatic relief for the symptoms of mild asthma. To date, patients suffering from mild asthma have had wide access to these products to provide relief, when necessary from mild asthma. If these products are reclassified to Category II, many patients will not have access to an OTC product as the single entity ephedrine products are not widely available in the commercial marketplace and will have to seek more costly treatment. In many instances, patients will forgo treating their mild asthma.

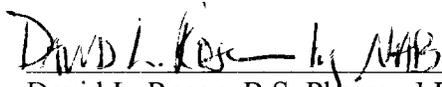
Again, the ACRC, requests that FDA stay finalization of the proposed reclassification; duly consider comments on the clinical evidence and analyses submitted by Bayer HealthCare Consumer Care Division on November 2, 2005 and Wyeth Consumer Healthcare on November 7, 2005 with respect to the medical rationale for combination therapy; and republish in the Federal Register, for further notice and comment revised conclusions with respect to ephedrine/guaifenesin combination products based on the Bayer and Wyeth data.

While the ACRC believes that the administrative record, as now supplemented with additional data and information to support the use of a bronchodilator and expectorant for the treatment of mild asthma, should the Agency believe that additional studies are necessary, it is prepared to conduct additional clinical research to demonstrate the existence of a meaningful target population and to further support the rationality, safety, and effectiveness of the products. Accordingly, should the FDA deem that additional studies are necessary to further support the

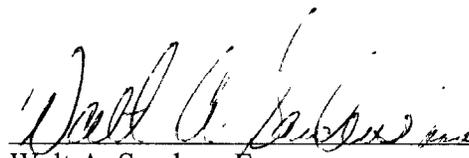
use of an expectorant in combination with a bronchodilator for use in the treatment of mild asthma, the ACRC is willing to meet with FDA officials in the Division of OTC Drug Products and the Division of Pulmonary and Allergy Drug Products to discuss the data necessary research designs and time schedules for completion of such studies. In such a situation, the ACRC requests that FDA stay final action on its proposal reclassifying pending the outcome of the requested meeting and FDA's review of the resulting data.

On behalf of the ACRC, we appreciate your consideration of these comments.

Sincerely yours,



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