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MCDERMOTT, WILL & EMERY

May 25, 2001

Docket Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

6051 01 MAY 29 P1:35

CITIZEN PETITION

The undersigned, submits this petition under the Federal Food, Drug, and Cosmetic Act §§ 201 et seq. and 21 C.F.R. § 10.30 to request the Commissioner of Food and Drugs ("Commissioner") take the following action:

A. Action Requested

1. Petitioner requests that the Commissioner amend 21 C.F.R. Part 341 - Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-The-Counter Human Use, specifically to include chewing gum as a delivery system for the release of the active ingredient menthol as a topical antitussive drug.

2. Based on the data appended hereto, the Petitioner requests the following regulations be amended [amended language in underlined type]:

OIP-0253

CP1

21 C.F.R. § 341.3(c)

(c) *Topical antitussive drug.* A drug that relieves cough when inhaled after being applied topically to the throat or chest in the form of an ointment or from a steam vaporizer, ~~or~~ when dissolved in the mouth in the form of a lozenge, or when released from a chewing gum for a local effect.

21 C.F.R. § 341.76 (c)(2)(iv)

(iv) For products containing menthol identified in § 341.14(b)(2) in chewing gum.

Two pieces of the product release between 5 to 10 milligrams of menthol in 20 minutes. Adults and children 2 to under 12 years of age: Chew 2 pieces of gum for approximately 20 minutes. May be repeated every hour as needed or as directed by a doctor. Children under 2 years of age: consult a doctor. Do not swallow chewing gum.

B. Statement of Grounds

1. Introduction

Petitioner seeks to amend the above monograph to encourage the development and sale of new and innovative methods for the delivery of drug products. It is in the public's best interest to be provided a wide variety of alternative choices of products that are each safe and effective. In the current instance, Petitioner will demonstrate through data amended hereto that the chewing gum delivery system provides an alternative dosage form and an equivalent amount of menthol, and therefore is a safe and effective delivery system for over-the-counter ("OTC") antitussive treatment.

2. The Current Monograph

On August 12, 1988, FDA published a final rule in the form of a final monograph establishing conditions under which OTC antitussive drug products are generally

recognized as safe and effective and not misbranded. 52 Fed. Reg. 30,042 (August 12, 1988). The monograph permits both oral and topical antitussive drug products. See 21 C.F.R. § 341.3. For topical antitussives the active ingredients camphor and menthol are each permitted. See 21 C.F.R. § 341.14. For topical antitussives, the use of menthol in a lozenge is permitted with the following directions:

The product contains 5 to 10 milligrams menthol. Adults and children 2 to under 12 years of age: Allow lozenge to dissolve slowly in the mouth. May be repeated every hour as needed or as directed by a doctor. Children under 2 years of age: consult a doctor.

21 C.F.R § 341.76(d)(2)(iii).

FDA has recognized the United States Pharmacopeia ("USP") definition of "lozenge:"

Lozenges are solid preparations, that are intended to dissolve or disintegrate slowly in the mouth. They contain one or more medicaments, usually in a flavored, sweetened base. They can be prepared by molding (gelatin and/or fused sucrose or sorbitol base) or by compression of sugar based tablets. Molded lozenges are sometimes referred to as pastilles while compressed lozenges are often referred to as troches. They are usually intended for treatment of local irritation or infections of the mouth or throat but may contain active ingredients intended for systemic absorption after swallowing.

"The United States Pharmacopeia 24_The National Formulary 19." The United States Pharmacopeial Convention, Inc., Rockville, MD, p. 2112, 2000.

In the preamble to the tentative final monograph ("TFM") for antitussive drug products, the agency noted that the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products ("the Panel") concluded that menthol is a peripherally acting agent which acts on the nerve receptors within the respiratory tract. See 48 Fed. Reg. 48,584, 48,588 (Oct. 19, 1983).¹ Both a lozenge and chewing gum

¹ The panel's description was as follows:

release menthol in a similar manner to act on the nerve receptors within the respiratory tract.

Chewing gum, like lozenges, is a recognized and well-accepted dosage form for OTC drug products. Numerous products including Nicorette® Gum, Biotene Dental Gum, and Aspergum (aspirin pain reliever gum tablets) are available for OTC use and have been demonstrated to be a safe and effective dosage form. Petitioner submits that chewing gum is an appropriate dosage for use in the antitussive portion of the Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Monograph.

3. **The Release Mechanism for Chewing Gum is Identical to Lozenges**

As described above, a menthol based lozenge is a peripherally acting agent. The data appended hereto, demonstrates that the active ingredient menthol, in a chewing gum is released at a comparable rate and extent as it is from menthol-containing lozenges. Upon chewing of the gum, menthol is released and is available for action on nerve receptors within the respiratory tract. Once the menthol is released from the dosage form (i.e., upon chewing the gum or from sucking on a lozenge) it is available for action on nerve receptors within the respiratory tract in an identical manner.

Peripherally acting antitussive agents act on the nerve receptors within the respiratory tract. Cough suppression may be produced by several different mechanisms such as a local anesthetic (pain deadening) or analgesic (pain suppressing) action on the mucosa of the respiratory tract; enhancing bronchial airway drainage by reducing the viscosity (thickness) of retained secretions, which may occur with effective expectorant agents or with adequate humidification of the airway; relaxation of the smooth muscle of the bronchial airway in the presence of spasm; or a soothing (demulcent) effect on the irritated throat and bronchial airway walls.

41 Fed. Reg. 38,312, 38,338 (recommendation of OTC panel).

4. **The Rate and Extent of Release of Menthol for Chewing Gum is Comparable to That of a Lozenge**

In addition to the method of release, the data demonstrates that the rate and extent of release is comparable to menthol-containing lozenges. Each piece of the chewing gum releases an average of 4.61 mg (SD 0.52) of menthol within the recommended chewing time of twenty minutes. The data from three leading brands of menthol-containing cough drops (lozenges) are enclosed and show that at 20 minutes, Robitussin, 5mg of menthol per cough drop, releases 4.23mg of menthol; Halls, 7.6mg of menthol per cough drop, releases 5.72mg of menthol; and Fisherman's, 10mg of menthol per cough drop, releases 5.95mg of menthol. (Release data reported are an average of a 6 lozenge composite sample.)

5. **The Proposed Labeling for This Product Is Compliant with the Monograph**

Proposed labeling for this product is included with this petition as an attachment. The proposed labeling is compliant with the monograph except for those changes proposed in this petition. For your convenience, I have also enclosed labeling from three national brands of lozenge products that contain menthol.

C. **Conclusion**

For the reasons identified above, Petitioner hereby requests that the Commissioner amend 21 C.F.R. Part 341 - Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-The-Counter Human Use as proposed.

D. **Environmental Impact**

Petitioner believes that this petition does not require an environmental impact analysis report under 21 C.F.R. § 25.1(g)(1995).

E. Economic Impact

An economic impact report is required only when requested by the Administration and such report has not been requested. 21 C.F.R. § 10.30(b).

CERTIFICATION

Petitioner certifies that, to the best of its knowledge and belief, this Petition includes all of the information and views on which the Petition relies and that it includes representative data and information known to the Petitioner which are unfavorable to the Petitioner.

Respectfully submitted,

A handwritten signature in black ink that reads "David L. Rosen". The signature is written in a cursive style with a large, sweeping initial "D".

David L. Rosen, R.Rh., J.D.