



October 28, 2002

Charles Ganley, M.D., Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research (HFD-560)
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Ganley:

I am in receipt of your letter of September 10, 2002. Your letter responded to my request of August 16, 2002 to meet with you to discuss the petition filed by the American Herbal Products Association and the International Aloe Science Council regarding FDA's final rule for aloe and cascara sagrada as ingredients in stimulant laxative OTC products.

I was disappointed that you denied my request for a meeting. It is my belief that a discussion in the format of a meeting would have value beyond that which can be gained simply by reviewing our petition and any additional information that might be submitted to the docket. Nevertheless, I must accept your decision in this matter, but respectfully request that you reconsider it at any time that would be convenient for you.

You suggested in your letter that we submit additional information relevant to our petition to Docket No. 78N-036L. We have submitted significant information to that docket today, in the form of eight (8) summaries of literature searches conducted over the past several months for publicly available

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information on cascara sagrada bark (*Frangula purshiana* = *Rhamnus purshiana*) and known components of cascara sagrada bark. We intend to also submit a review document within the next several weeks that will evaluate the relevance of the data presented in these literature searches as it pertains to a thorough review of the potential mutagenicity, genotoxicity, and carcinogenicity of cascara sagrada ingredients.

Please do not hesitate to contact me to discuss this matter.

Sincerely,


Michael McGuffin
President

Docket No. 78N-036L

**BEFORE THE
UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

SUBMISSION OF ADDITIONAL INFORMATION
ON THE STATUS OF
CASCARA SAGRADA INGREDIENTS
AS OVER-THE-COUNTER DRUG ACTIVE INGREDIENTS

BY THE
AMERICAN HERBAL PRODUCTS ASSOCIATION**

October 28, 2002

The American Herbal Products Association (AHPA) hereby submits additional information to Docket No. 78N-036L that is relevant to the status of cascara sagrada ingredients as active ingredients in stimulant laxative over-the-counter drug products.

This submission consists of eight (8) summaries of literature searches conducted over the past several months for publicly available information on cascara sagrada bark (*Frangula purshiana* = *Rhamnus purshiana*) and known components of cascara sagrada bark. The subjects of these literature searches include: aloe-emodin (CAS Registry No. 481-72-1); barbaloin (1415-73-2); casanthranol 8024-48-4); cascara (8047-27-6); cascaroside (50814-04-5); chrysaloin (no CAS Registry No.); chrysophanol (481-74-3); and emodin (518-82-1).

AHPA and the International Aloe Science Council (IASC) on June 10, 2002 submitted a petition to request a stay and reconsideration of the provisions of 21 C.F.R. § 310.545(a)(12)(iv)(C) and (d) regarding the status of aloe vera ingredients (aloe, aloe extract, aloe flower extract) and cascara sagrada ingredients (casanthranol, cascara fluidextract aromatic, cascara sagrada bark, cascara sagrada extract, cascara sagrada fluidextract) which were purportedly made final in a Federal Register notice published May 9, 2002 (67 Fed. Reg. 31125). The relief requested was that the Food and Drug Administration (“agency”) stay the November 5, 2002 effective date of this regulation and that the agency reconsider the regulation in light of new information not previously considered by the agency or its Advisory Review Panel on OTC Laxative,

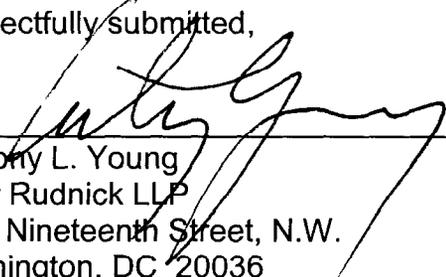
Antidiarrheal, Emetic, and Antiemetic Drug Products or, insofar as the associations are aware, by its OTC Drug Product staff. The submission made to this docket today is part of that information not previously considered by these parties for cascara sagrada.

In a notice in the *Federal Register* of June 19, 1998 (63 FR 33592) FDA reopened the administrative record and reclassified several stimulant laxative ingredients, including those that are derived from cascara sagrada, from Category I (monograph) to Category III (more data needed). The agency stated that it had not received any mutagenicity, genotoxicity, and carcinogenicity data for cascara sagrada ingredients. AHPA believes that the information submitted herewith represents such data.

AHPA intends to submit a review document within the next several weeks that will evaluate the relevance of the data presented in these literature searches as it pertains to a thorough review of the potential mutagenicity, genotoxicity, and carcinogenicity of cascara sagrada ingredients.

This submission of additional information is made without waiver of the positions set forth in AHPA's petition for stay and reconsideration.

Respectfully submitted,



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