BEFORE

THE UNITED STATES OF AMERICA

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH
NATIONAL TOXICOLOGY PROGRAM
OFFICE OF THE REPORT ON CARCINOGENS

COMMENTS OF THE

AMERICAN HERBAL PRODUCTS ASSOCIATION
AND THE
INTERNATIONAL ALOE SCIENCE COUNCIL

ON

Request for Information on Nominations for the Report on Carcinogens (RoC):

Aloe vera

October 18, 2013

The American Herbal Products Association (AHPA) is the national trade association and voice of the herbal products industry, comprised of companies doing business as growers, processors, manufacturers, and marketers of herbs and herbal products, including herbal supplements and other dietary supplements. AHPA serves its members by promoting the responsible commerce of products that contain herbs, including dietary supplements.

The International Aloe Science Council (IASC) is the trade association representing businesses growing, supplying and marketing products containing aloe vera, including foods, dietary supplements, and personal care items.

Many of AHPA's members and the vast majority of IASC's members are businesses that either sell aloe vera (*Aloe vera*) raw materials or that market consumer goods containing aloe vera leaf derived ingredients, though very few to none are engaged in selling products for oral consumption containing the NTP study material identified as *Aloe vera* nondecolorized whole leaf.

Background and subject of these comments

In a Federal Register notice dated September 20, 2013 (the September 20 notice) the National Toxicology Program (NTP) requested information on several substances that have been nominated for possible review for future editions of the Report on Carcinogens (RoC), including the substance identified in the September 20 notice as "Aloe vera whole leaf extract *(Aloe barbadensis* Miller)*"*

In the September 20 notice NTP requested certain specific information on each of these substances, including data on current production, use patterns, and human exposure; information about published, ongoing, or planned studies related to evaluating carcinogenicity; scientific issues important for assessing carcinogenicity of the substance; and names of scientists with expertise or knowledge about the substance.

These comments provide information in each of these areas for aloe vera.

<u>Scientific issues important for assessing carcinogenicity.</u>

- *Additional detail is necessary to clearly characterize and differentiate the substance of interest from the aloe vera ingredient(s) predominantly available in the marketplace.*

NTP conducted a 2-year feeding study on a specific extract of aloe vera leaf that had been subjected to only very minimal processing. The results of this study were recorded in NTP Technical Report 577 (NTP TR 577), dated August 2013. NTP TR 577 clearly and properly identifies the substance studied as "a nondecolorized whole leaf extract of *Aloe Barbadensis* [sic] Miller (Aloe Vera)." The tested substance was reported to contain 10,000-13,000 ppm aloin, and NTP TR 577 is titled to clearly define the tested substance as "nondecolorized." This is important as it clearly differentiates the NTP tested substance from other aloe vera leaf extracts available in the marketplace. AHPA and IASC strongly encourage NTP to continue to use precise nomenclature in any publication on and discussion of aloe vera leaf extracts, including in publications and discussions relevant to the RoC.

The vast majority of aloe vera leaf extract products available in the marketplace are made with aloe vera ingredients virtually devoid of aloin and other laxative agents naturally-occurring in the latex in aloe vera leaf. This purification is accomplished via a decolorization process, a video of which produced by the IASC can be viewed HERE. This process uses an activated carbon (activated charcoal) filtration step to remove anthrones and anthraquinones, known hazards found in aloe latex.

- *There are several different raw materials ingredients that can be made from* Aloe vera *leaf.*

  There are two primary types of processed raw ingredients used in commercially available aloe vera leaf beverage products:

  - Decolorized or purified aloe vera leaf juice ("leaf," sometimes also referred to as "whole leaf").
  - Aloe vera inner leaf juice ("inner leaf," sometimes also referred to as "inner filet" or "gel").

  Unpurified leaf juice containing high levels of the latex is not a common commercial item and, like the stimulant laxatives made with "drug aloe," may contain significant amounts of aloe latex, the bitter, yellow sap found between the rind and the inner leaf material.

  A complete description of the above, including flow charts of how the various aloe vera raw materials are processed, can be found in the Encyclopedia of Dietary Supplements, 2nd Edition chapter on aloe vera.

Knowledgeable scientists. AHPA and IASC have identified the following as scientists having significant expertise and knowledge regarding *Aloe vera*.

- Vasilios Frankos, Ph.D., Senior Vice President Global Product Science Safety & Compliance, Herbalife International of America, Inc., 990 West 190th St., Suite 650 Torrance, CA 90502. His *curriculum vitae* is appended to these comments; he can be contacted at vfrankos@herbalife.com.
- Kenneth Jones, B.Sc., Chief Operations Officer, Aloecorp, 2660 Willamette Dr., Lacey, WA 98516. His *curriculum vitae* is appended to these comments; he can be contacted at kenj@aloecorp.com.

Data on current production, use patterns, and human exposure. IASC has produced a market survey that offers quantitative information on aloe vera juice raw materials sold from 2009-2010 for the various aloe vera ingredient types predominantly available. This data demonstrates that the vast majority of commercially available aloe vera material is decolorized or otherwise contains less than 10ppm of aloin.

Studies evaluating carcinogenicity of products containing decolorized (purified) whole leaf and inner leaf aloe vera juice. AHPA and IASC are aware of several, recent animal studies that evaluated the carcinogenicity of products containing decolorized (or purified) leaf juice and inner leaf juice. These studies have been published in peer-reviewed journals and are outlined below:

- Sehgal I, Winters WD, Scott M, Kousoulas K. An in vitro and in vivo toxicologic evaluation of a stabilized aloe vera gel supplement drink in mice. *Food Chem Toxicol*. 2013 May,55:363-370.
- Sehgal I, Winters WD, Scott M, David A, Gillis G, Stoufflet T, Nair A, Kousoulas K. Toxicologic assessment of a commercial decolorized whole leaf aloe vera juice, Lily of the Desert filtered whole leaf juice with aloesorb. *J Toxicol*. 2013. Doi: 10.115/2013/802453. Epub 2013 Mar 11
- Shao A, Broadmeadow A, Godard G, Bejar E, Frankos V. Safety of purified decolorized (low anthraquinone) whole leaf Aloe vera (L.) Burm. f. juice in a 3-month drinking water toxicity study in F44 rats. *Food Chem Toxicol*. 2013 Mar 14;57C:21-31
- Williams LD, Burdock GA, Shin E, Kim S, Jo TH, Jones KN, Matulka RA. Safety studies conducted on a proprietary high-purity aloe vera inner leaf fillet preparation, Qmatrix. *Regul Toxicol Pharmacol.* 2010 Jun;57(1):90-8. doi: 10.1016/j.yrtph.2010.01.002. Epub 2010 Jan 22.

AHPA and IASC appreciate the opportunity to provide these comments. Please feel free to contact us if additional information or clarification is needed.

Respectfully submitted,

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