

April 28, 2005

Dr. Susan J. Walker
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Center for Food Safety and Applied Nutrition
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MAY - 5

FDA / VL

RE: FDA Response Letter for New Dietary Ingredient Notification [Kaneka Glavonoid Rich Oil Brand of Licorice Flavonoid Oil (LFO)]

Dear Dr. Walker:

I received your letter of February 18, 2005 concerning the Agency's review of the New Dietary Ingredient (NDI) notification for Kaneka Glavonoid Rich Oil Brand of Licorice Flavonoid Oil (LFO). The original NDI notification, dated December 6, 2004, included summaries of the information forming the basis of our conclusion that the substance does not pose an unreasonable risk of harm. The agency indicated in the letter of February 18, 2005 that it had concerns about the evidence upon which this conclusion was based. In a conference call between representatives of FDA (Linda S. Pellicore, Ph.D and Ms. Vickey Lutwak) and Kaneka representatives on March 7, 2005, specific areas considered to be deficient in the original application were identified.

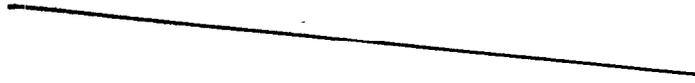
Pursuant to that discussion, CANTOX respectfully submits an amended NDI for Kaneka Glavonoid Rich Oil Brand of Licorice Flavonoid Oil (LFO). Enclosed is the complete version of this notification, in which additional information and clarification is provided to address the previous concerns of the Agency. In addition, an overview of these changes is provided herein and a red-lined version highlighting these changes is included as an attachment.

Dr. Pellicore requested additional clarification and information related to the following:

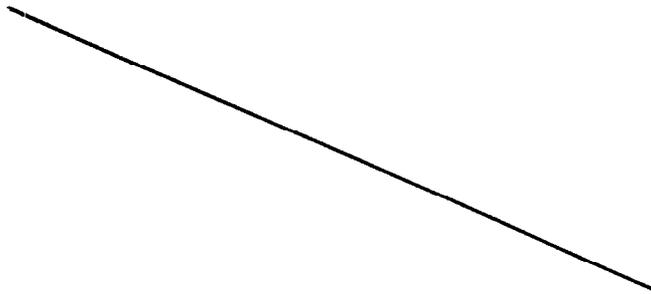
1. A specification for glycyrrhizinic acid in the LFO product;
2. Clarification regarding the composition of the "LFO concentrate solution" used in the non-clinical and genotoxicity studies and its relationship to the final LFO product;
3. Clarification of the relationship between the test materials used in the published studies and LFO;
4. A statement added to the conclusion that Kaneka LFO is safe for long-term (*i.e.*, chronic) use with general references to the supporting data.

The following are responses to each of the areas identified above; the amended NDI submitted herewith reflects these responses in greater detail.

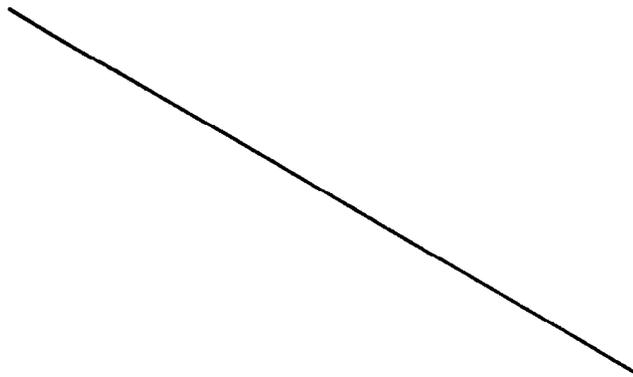
1.



2.



3.



4. The following statement was added to the conclusion

“Based on the evidence summarized above, including results of preclinical safety studies conducted on LFO concentrate, presence of a safety factor 120- to 180-fold that exists between the NOAELs from the 90-day repeated dose toxicity study and the maximum recommended dose to consumers (600 mg/day LFO, equivalent to 10 mg LFO/kg b.w. for a 60 kg b.w. person) and clinical studies of deglycyrrhizinated licorice, which like LFO,  showed that the test material generally had no adverse effects, Kaneka’s concludes that the chronic use of LFO in dietary supplements

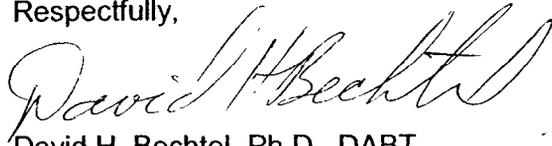
at a level of 600 mg per serving _____ will
be reasonably expected to be safe.” (page 57).

Having provided these clarifications to address the specific concerns of the agency, CANTOX and Kaneka reaffirm their original assertion that a dietary supplement containing Kaneka Glavonoid Rich Oil Brand of Licorice Flavonoid Oil (LFO) would reasonably be expected to be safe when used according to the conditions of use recommended or suggested in the labeling of the dietary supplement. Such usage would result in a maximum daily intake 600 mg/day LFO, equivalent to 10 mg LFO/kg bw for a 60 kg bw person, a level that can reasonably be expected to be safe based on the available data.

On behalf of Kaneka Corporation, CANTOX hereby confirms that this letter and the enclosed Notification contain trade secret or otherwise confidential commercial information which should not be disclosed to the public pursuant to 21 C.F.R. §§20.61 and 190.6(e). More specifically, the Notification contains valuable data and information which Kaneka Corporation has held in strict confidence and has not disclosed to any member of the public. If it would assist the staff, CANTOX or Kaneka will submit redacted copies of this letter and Notification, specifically identifying such confidential and proprietary information.

We respectfully submit that the revised notification fully responds to the Agency's concerns and is consistent with the discussion during the March 7, 2005 conference call with the Agency staff. We appreciate the staff's input and hope that the revised submission will facilitate the staff's prompt review of the revised Notification.

Respectfully,



David H. Bechtel, Ph.D., DABT
Managing Director & Sr. Scientific Consultant

Enclosures