DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Memorandum

Date November 4, 1993

From Additives Evaluation Branch No.1 (HFS-226)

Subject Revised ADI for sucrose fatty acid esters (SFAE), conclusions of meeting held Oct 5, 1993, and safety evaluation of pending petitions.

To Novel Ingredients Branch (HFS-207)
Attn: B. Anderson/ M.Cheeseman /D. Keefe
Through Kirk Biddle, Ph.D. Kirk Biddle
Chief, Additives Evaluation Branch No. 1 (HFS-226)

Food Additive Petition Nos. 0A4183 Mitsubishi Kasei Corp.
2A4321
9A4166 Nebraska Dept. of Economic Development

In the initial evaluation of SFAE in FAP No. 1A 3564, the ADI for SFAE was determined as 450 mg/p/day for a 60 kg individual. This ADI was based on the dog as the most sensitive species using soft stools as the endpoint, and a safety factor of 10 (since the product is hydrolyzed to normal food constituents before absorption) with 0.3 % as the NOEL. We have reexamined the study reports on which the NOEL is based.

In our March 15, 1993 memorandum re: the safety of SFAE we stated: we set the no-effect level (NOEL) for sucrose fatty acid esters (SFAE) in the dog as 1.0% dietary level based on diarrhea as an endpoint.

The study report, on a 26 - week feeding study of mixed sucrose esters of palmitic and stearic acid, a GLP study conducted by Huntingdon Research Centre, and reported in FAP 1A3564 states:

"A dosage-related increase was evident in the incidence of abnormally soft faeces recorded for animals receiving the 1.0% or 3.0% diet. The incidence of this finding in animals receiving 0.3 % diet, however, was comparable to that of control animals." Thus control animals as well as dosed animals exhibited soft feces.

The report continues: " A moderate reduction in the incidence of abnormally soft feces was evident in the control, 0.3 % and 1.0% groups during the second half of the treatment period, while only a slight reduction was recorded in the 3.0 % group over the same period. " The dogs of the low and intermediate dose level groups thus adapted to the high SFAE dietary levels in the course of the study.

These data were confounded by an incident of misdosing over 2 days on week 20 of the study which recorded an increase of the incidence of liquid or soft feces for animals receiving the 1.0 % diet, while coincidentally, a decrease in this clinical sign for animals receiving the 3.0 % diet. As a precaution, the report states, a new batch of diet was formulated for the remainder of the dosing week. Analysis of the diets confirmed that the high-dose group received the 1.0 % diet for these 2 days and the intermediate dose-group received the 3.0 % diet.

We base the NOEL on frank diarrhea because of the evaluation by Dr. Barker in which she states diarrhea is an adverse effect. Diarrhea was a dose-related response of SFAE overtly noted at the 3% dietary level in the dog studies. However, we noted that histopathologically, the large intestine was reported to be normal in both the 6-month study of mixed esters of sucrose palmitate and stearate and the one year study of sucrose palmitate at the 1% dietary level.

We have previously noted that sucrose fatty acid esters are hydrolyzed in the intestine to sucrose and fatty acids, which are normal constituents of the diet. The NOEL of 1 % in the diet translates into 1500 mg/p/day as the ADI for a 60 kg adult using a 10X safety factor based on the hydrolysis of SFAE prior to its absorption. The ADI for the 2-5 yr. age group would be based on a 15 kg individual. This may be calculated as 375 mg/p/d.

CRB (M. DiNovi, personal communication, 5/12/93) states that the EDI estimate includes all products that may be made using SFAE, although competing food emulsifiers may be used for the same purpose. A reasonable consumption figure would be a fraction of the calculated EDI based on all products approved for its incorporation.

Ms. Anderson and Dr. Keefe reported at the meeting of Oct. 5, 1993 (see Memorandum Of Conference, Oct 5, 1993) that none of the petitioners have provided information that reflect on the consumption of SFAE in the U.S. Dr. DiNovi reported that although the 1987 NAS Food Disappearance Survey lists SFAE in the U.S. food supply as zero, he pointed out that the Division of. Product Manufacture and Use (DPMU) bases its EDI on the assumption that the additive will have 100 % market penetration for its intended use. It was agreed at the meeting of Oct. 5, 1993 that

the total reasonable consumption figure would be under the ADI.

The issue of an EDI for the 2 to 5 year age group was also discussed in the in-house conference held Oct 5, 1993 (see memo of Conference op. cit.). It was concluded that because the petitioned uses for SFAE are in surimi, chewing gum, and as emulsifiers in ready-to -drink coffee and tea beverages; and since the 90th percentile intake (EDI) for toddlers are extremely small (surimi 0.1 mg/p/d, and chewing gum 1.9 mg/p/d; DiNovi, memo of 6/3/92) approval of these uses of SFAE will only negligibly increase the level of SFAE in this age group.

The proposed new uses of SFAE are safe because the 90th percentile cumulative consumption level (EDI) for SFAE as estimated by Chemistry Review Branch (CRB, HFS-247) is 718 mg/p/day and the ADI for adults is now considered to be 1500 mg/p/d. The additional intake by the 2 - 5 yr age group will be extremely small (2 mg/p/d) as compared to the ADI for this age group (375 mg/-p/d). On this basis we find the petitions acceptable and ready for regulation.

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CC:HFS-200, HFS-225, HFS-226(Biddle), HFS-247 (Edwards)
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