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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date May 3, 1994

AD

From Chemistry Review Branch, HFS-247

Subject FAP 4A4419 (MATS# 763, M2.1.1) - Kuraray International Corporation. Submission dated 4-7-94. Request of 4-20-94 from Indirect Additives Branch: Estimated exposure to 1,3-butadiene from the use of synthetic *n*-octanol.

To Indirect Additives Branch, HFS-216
Attn: R. Angeles, Ph.D.

Kuraray International is proposing to amend 21 CFR 172.864 (Synthetic fatty alcohols). The amendment would permit the safe use of *n*-octanol prepared from the hydro-dimerization of 1,3-butadiene. (Two other manufacturing processes are currently described in this regulation for production of *n*-octanol.) You have requested that we provide an estimate of consumer exposure to residual 1,3-butadiene from the use of Kuraray's synthetic *n*-octanol.

Background

n-Octanol is presently widely regulated for direct and indirect uses as follows: (1) as a defoamer in the manufacture of microcapsules for flavoring oils under §172.230 (Microcapsules for flavoring oils), (2) §172.515 (Synthetic flavoring substances and adjuvants), (3) for reaction with acids listed for phenolic resins under §175.300 in the following regulations: §175.105 (Adhesives), §175.300 (Resinous and polymeric coatings), §175.380 (Xylene-formaldehyde resins condensed with 4,4'-isopropylidenediphenol epichlorohydrin epoxy resins), §175.390 (Zinc-silicon dioxide matrix coatings), §176.170 (Components of paper and paperboard in contact with aqueous and fatty foods), and §177.1210 (Closures with sealing gaskets for food containers), (4) for general use in the following regulations: §175.300, §175.380, §175.390, §176.170, §177.1210, and §177.1350 (Ethylene-vinyl acetate copolymers), (5) §177.1200 (Cellophane) and §177.1400 (Water-insoluble hydroxyethyl cellulose) as a defoaming agent in the manufacture of base sheet, and (6) §178.3480 (Synthetic fatty alcohols).

Under §172.864 and by cross-reference to §178.3480, synthetic *n*-octanol may be used as a substitute for *n*-octanol derived from naturally occurring fatty alcohols permitted in food and as components of food-contact articles and as an intermediate in the synthesis of food additives and other substances permitted as components of food-contact articles. Since *n*-octanol, prepared by the hydro-dimerization of 1,3-butadiene, is to replace naturally derived and other synthetic *n*-octanol, the overall exposure to *n*-octanol is not expected to increase as a result of regulation of this petition. However, in order to estimate exposure to 1,3-butadiene from the use of this synthetically derived *n*-octanol, an estimate of exposure to *n*-octanol from all its regulated uses must be determined. Then, by multiplying the estimated daily intake (EDI) of *n*-octanol for each use by the detection limit for residual 1,3-butadiene (< 1 ppm, as supported by the present petition), an upper-limit EDI of residual 1,3-butadiene from use of *n*-octanol can be calculated.

Previously (memorandum of 4-14-94, R. McDaniel to T. Brown), CRB calculated a cumulative exposure to residual 1,3-butadiene that might result from regulation of five pending indirect additive petitions (FAPs 2B3620, 8B4083, 1B4256, 2B4337, and 3B4377). The cumulative exposure (0.87 μg/p/d) was described as extremely conservative because exposure values calculated for three of the five pending petitions were based on detection threshold values rather than reports of detected 1,3-butadiene. All calculations assumed 100% migration of residual 1,3-butadiene to food.

Exposure to *n*-Octanol and 1,3-Butadiene

From Use in Microcapsules

The estimated daily intake (EDI) of *n*-octanol from its use as a defoamer in the manufacture of microcapsules for flavoring oils (§172.230) may be calculated based on information provided in FAP 8A2199. The petitioner provided a list of foods that may use flavor microcapsules and the expected use level of the microcapsules in those foods (see memorandum of 2-19-1968, M. Prochazka to W. Schaefer), which is tabulated below. The petitioner states that *n*-octanol is present at no greater than 50 ppm in microcapsules. By multiplying the use level of the microcapsules in a food by the maximum level of *n*-octanol that might be present in the microcapsules (50 ppm), an upper-limit concentration of *n*-octanol in each food can be calculated. These values are also listed below.

Food	Use Level of Microcapsule in Food (mg/g)	Upper-Limit Concentration of *n*-Octanol in Food (μg/g)
cake mixes	0.66	0.03
pudding powder	0.66	0.03
gelatin dessert mix	0.15	0.008
chewing gum	6.0	0.3
cookies	0.66	0.03
taffy candy	0.66	0.03

The mean intake and % eaters of each food (the percent of the population that consumed each food listed at least once during the survey period) was taken from the 1982 -1987 Market Research Corporation of America (MRCA) five year Menu Census (1987/88 USDA/NFCS for portion size) based on eaters-only data and are tabulated below. The total-sample mean intake

of each food is calculated by multiplying the eaters-only mean intake for each food by the percent of the population that consumed each food at least once during the survey period.

Food (GRAS Food Category)	Eaters-Only Mean Intake (g/p/d)	% Eaters	Total-Sample Mean Intake g/p/d
cake mixes (01P1)	20	39	7.8
pudding powder (20D2)	22	7	1.5
gelatin dessert mix (20A2)	24	25	6.0
chewing gum (31)	2	14	0.3
cookies (01L1)	10	60	6.0
taffy candy (16H1)	6	11	0.7

By multiplying the total-sample mean intake of a food by the concentration of *n*-octanol in that food, the total-sample mean EDI of *n*-octanol from the consumption of each food can be calculated. The total-sample mean EDI of residual 1,3-butadiene from the consumption of each food is then calculated by multiplying the total-sample EDI of *n*-octanol by 1 ppm (the detection limit of residual 1,3-butadiene in *n*-octanol). These values are tabulated below.

Food	Total-Sample Mean EDI of *n*-Octanol (μg/p/d)	Total-Sample Mean EDI of 1,3-Butadiene (pg/p/d)
cake mixes	0.2	0.2
pudding powder	0.05	0.05
gelatin dessert mix	0.05	0.05
chewing gum	0.09	0.09
cookies	0.2	0.2
taffy candy	0.02	0.02

The calculated total-sample mean EDI for residual 1,3-butadiene from each of the foods is then summed to obtain the cumulative total-sample mean EDI for residual 1,3-butadiene (**0.6 pg/p/d**). To calculate the mean cumulative eaters-only EDI for residual 1,3-butadiene, the cumulative total-sample mean EDI for residual 1,3-butadiene is divided by the % eaters of all of these foods (87%).[1] The mean cumulative eaters-only EDI for residual 1,3-butadiene is 0.7 pg/p/d.

From Use as a Flavoring Substances and Adjuvant

In order to calculate exposure to residual 1,3-butadiene from the use of *n*-octanol as a flavoring agent in food, we have relied on information obtained from the Flavor and Extract Manufacturers' Association (FEMA)/Research Institute for Fragrance Materials (RIFM) database on use levels of *n*-octanol in food (see fax of 4-21-94, J. Griffiths to R. McDaniel). Tabulated below are the foods containing *n*-octanol and the average use level of *n*-octanol in those foods. The mean intake of each food and % eaters was taken from the 1982 - 1987 MRCA five year Menu Census (1987/88 USDA/NFCS for portion size) based on eaters-only data and are tabulated below. The total-sample mean intake for each food is calculated by multiplying the eaters-only mean intake for each food by the percent of the population that consumed each food at least once during the survey period.

[1] % eaters $= [1 - \prod_{i=1}^{\infty} (1 - \xi_i)] \times 100$ where ξ_i is the fraction of eaters of food i.

Food (GRAS Category)	% Eaters	Eaters-Only Mean Intake (g/p/d)	Total-Sample Mean Intake (mg/p/d)	Concentration of *n*-Octanol (ppm)
baked goods (01)	99.9	131	131	7.2
frozen dairy (07)	71	39	28	4.4
meat products (10)	99.6	159	159	0.3
soft candy (16G)	8	2	0.2	4.3
gelatin pudding custard (20)	46	34	16	3.2
non-alcoholic beverages (23)	86	241	207	1.4
hard candy (16F)	9	3	0.3	0.6
chewing gum (31)	14	2	0.3	6.4

By multiplying the total-sample mean intake of a food by the use level of *n*-octanol in that food, the total-sample mean EDI of *n*-octanol from the consumption of each food can be calculated. The total-sample mean EDI of residual 1,3-butadiene from the consumption of each food is then

calculated by multiplying the total-sample mean EDI of *n*-octanol by 1 ppm (the detection limit of residual 1,3-butadiene in *n*-octanol). These values are tabulated below.

Food	Total-Sample Mean EDI of *n*-Octanol (mg/p/d)	Total-Sample Mean EDI of 1,3-Butadiene (ng/p/d)
baked goods	0.94	0.94
frozen dairy	0.12	0.12
meat products	0.048	0.048
soft candy	0.009	0.009
gelatin/pudding/ custard	0.051	0.051
nonalcoholic beverages	0.29	0.29
hard candy	0.0002	0.0002
chewing gum	0.002	0.002

The calculated total-sample mean EDI for residual 1,3-butadiene from each of the foods is then summed to obtain the cumulative total-sample mean EDI for residual 1,3-butadiene (**1.5 ng/p/d**). To calculate the cumulative eaters-only EDI for residual 1,3-butadiene, the cumulative total-sample mean EDI for residual 1,3-butadiene is divided by the % eaters of all of these foods ($\approx$ 1). The cumulative eaters-only EDI for residual 1,3-butadiene is 1.5 ng/p/d.

From Indirect Uses

Exposure to *n*-octanol from its use as a defoaming agent in cellophane and water insoluble hydroxyethyl cellulose (§177.1200 and §177.1400) was calculated in FAP 5B1761 (see memorandum of 11-24-65, E. Detwiler to W. Schaefer). The concentration in food of *n*-octanol, based on 100% migration, was determined to be 2.3 ppm. Using a consumption factor (CF) of 0.05 for cellophane, the dietary concentration of *n*-octanol from its use as a defoaming agent is 0.12 ppm. The EDI of *n*-octanol is:

$$\text{EDI} = 3000 \text{ g/p/d} \times 0.12 \times 10^{-6} \text{ g/g}$$

$$= 0.36 \text{ mg/p/d}$$

The EDI of residual 1,3-butadiene from the use of *n*-octanol as a defoaming agent is then calculated by multiplying the EDI of *n*-octanol (0.36 mg/p/d) by the detection limit of residual 1,3-butadiene (1 ppm). The EDI of residual 1,3-butadiene from this use of *n*-octanol is 0.36 ng/p/d.

The food additive petitions from which the remaining indirect uses of *n*-octanol (cited previously) are derived do not contain sufficient information to calculate an exposure to *n*-octanol, and thus, an exposure to residual 1,3-butadiene. Products derived from 1,3-butadiene are also regulated under each of these indirect regulations (§175.105, §175.300, §175.380, §175.390, §176.170, and §177.1210) and *n*-octanol is cleared for use as a synthetic intermediate in the synthesis of substances permitted as components of food-contact articles in all of these indirect regulations. Therefore, we would expect that exposure to residual 1,3-butadiene found in products derived **directly** from 1,3-butadiene (*e.g.*, butadiene-containing polymers) would be significantly greater than exposure to residual 1,3-butadiene resulting from the use of *n*-octanol contaminated with residual 1,3-butadiene (*e.g.*, cellulose made with *n*-octanol defoamer contaminated with residual 1,3-butadiene). Therefore, consumer exposure to residual 1,3-butadiene from the uses of *n*-octanol described in this memorandum will be negligible when compared to the predicted exposure of 0.87 μg/p/d from the petitioned indirect additive uses reviewed in our memorandum of 4-12-94.

Summary

The predicted EDI to residual 1,3-butadiene that might result from regulation of this petition for synthetic *n*-octanol is 1.5 ng/p/d with flavor use of *n*-octanol as the principle source.

The consumer exposure to residual 1,3-butadiene from the use of synthetic *n*-octanol manufactured by the hydro-dimerization of 1,3-butadiene is negligible when compared to the predicted exposure of 0.87 μg/p/d from the presently pending unregulated indirect additive petitions (FAPs 2B3620, 8B4083, 1B4256, 2B4337, and 3B4377; see memorandum of 4-12-94, R. McDaniel to T. Brown).

Roseann F. McDaniel, Ph.D.

HFS-226; 245; 248 (Hollifield); 247 (Kuznesof)
HFS-247:RFMcDaniel:254-9537:rfm:butcumb.mem:4-26-94, 5-2-94
RD Init:MAAdams, 5-2-94
PMKuznesof, 5-3-94