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Memorandum

Date July 26, 1994

From Chemistry Review Branch, HFS-247

Subject FAP 4A4419 (MATS #763, M2.1) - Kuraray International Corporation/Keller & Heckman. Submissions dated 4-7-94 and 4-12-94. *n*-Octanol via a new manufacturing process.

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

AD



Keller & Heckman, on behalf of Kuraray International, has proposed to amend 21 CFR 172.864 (Synthetic fatty alcohols) to permit the safe use of *n*-octanol prepared by the hydro-dimerization of 1,3-butadiene. (Two other manufacturing processes for production of *n*-octanol are currently described in this regulation.) Their synthetic *n*-octanol is intended to replace naturally derived and other synthetic *n*-octanol.

Identity and Manufacture

CAS Name: octan-1-ol

Common Names: 1-octanol

n-octanol

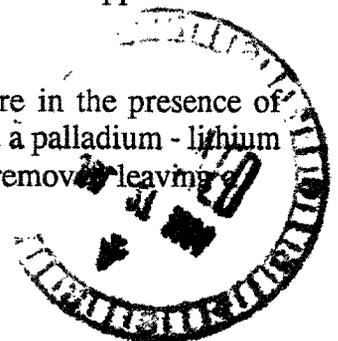
caprylic alcohol

CAS Registry Number: 111-87-5

Empirical Formula: C₈H₁₈OStructure: CH₃CH₂CH₂CH₂CH₂CH₂CH₂CH₂OH

An infrared spectrum, which supports the structure of *n*-octanol, is included in Appendix II on pp. 000048 - 000050.

n-Octanol is produced by the dimerization of 1,3-butadiene under pressure in the presence of sulfolane (a polymerization solvent), water, triethylamine, bicarbonate, and a palladium - lithium catalyst. The reaction mixture is extracted with hexane. The hexane is removed leaving



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mixture of 92% octa-2,7-dien-1-ol and 4% octa-1,7-dien-3-ol. The dienols are hydrogenated with a nickel catalyst and purified by distillation.

The specifications for the raw materials used in the production of the additive are listed in Appendix III on pp. 000055 - 000062. The specifications for the additive are listed on p. 000014 and in Appendix III on p. 000063. The analytical procedures for determining compliance with these specifications are outlined in Appendix III on pp. 000064 - 000069. To demonstrate that the additive meets the petitioner's specifications, analysis of three batches of *n*-octanol were provided (p. 000015).

The petitioner states that four impurities are present in their *n*-octanol. The identity and amount of these impurities in *n*-octanol are tabulated below:

<u>Compound</u>	<u>Weight % in <i>n</i>-Octanol</u>
3-octanol	0.11
diethyloctylamine	0.10
dioctylether	< 0.001
2-hexyldecyloctylether	< 0.001

The petitioner has also analyzed *n*-octanol for residual 1,3-butadiene. The analytical method (described on p. 000070) is sensitive to 1 ppm of 1,3-butadiene. As demonstrated in the chromatograms on pp. 000071 - 000077, no 1,3-butadiene was detected at the limit of detection in three batches of *n*-octanol.

Use

The petitioner's *n*-octanol is intended for use as a substitute for currently regulated synthetic and naturally derived *n*-octanol permitted in food and as components of food-contact articles and as intermediates in the synthesis of food additives and other substances permitted as components of food-contact articles. The regulated uses are outlined in our previous memorandum concerning this petition (see memorandum of 5-3-94, R. McDaniel to R. Angeles).

Exposure

To *n*-Octanol and 1,3-Butadiene

The petitioner states that 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. We agree with this

statement. Nevertheless, the petitioner has calculated the dietary concentration of *n*-octanol to be < 9.2 ppb, based on *per capita* disappearance of *n*-octanol and several other alcohols. The dietary concentration was determined by summing the poundage¹ of eight fatty alcohols (5,534 lbs for 1-octanol, 2-octanol, 3-octanol, 1-decanol, lauryl alcohol, myristyl alcohol, 1-hexadecanol, and stearyl alcohol) and converting it to dietary concentration as follows:

$$\frac{5,534 \text{ lbs alcohol/yr} \times 453 \text{ g/lb}}{3000 \text{ g food/person/d} \times 250 \times 10^6 \text{ people} \times 365 \text{ d/yr}} = \frac{9.2 \times 10^9 \text{ g alcohol}}{\text{g food}} = 9.2 \text{ ppb}$$

The dietary concentration of 1,3-butadiene, a potential contaminant of *n*-octanol, was calculated by multiplying the dietary concentration of *n*-octanol (9.2×10^9 g/g) by the limit of detection for residual 1,3-butadiene (< 1 ppm). The dietary concentration of 1,3-butadiene from the use of *n*-octanol is calculated to be 9.2×10^{15} g/g or 9.2 ppquadrillion.

It should be noted that the petitioner's calculations, by including alcohols other than *n*-octanol, represent an overestimation of the amount of *n*-octanol and 1,3-butadiene entering the food supply. The petitioner's use of a *per capita* estimate will, however, result in a significant underestimate of actual dietary concentration and EDI. Therefore, we prepared an estimate of daily intake more reflective of actual consumer exposure. Our exposure calculations for *n*-octanol and 1,3-butadiene were presented in our memorandum of 5-3-94 concerning this petition (R. McDaniel to R. Angeles). We agree that the overall exposure to *n*-octanol would not increase as a result of regulation of this petition. Evaluating the regulated uses of *n*-octanol, we determined that the estimated daily intake (EDI) of *n*-octanol from its use in microcapsules is 0.61 $\mu\text{g/p/d}$, from its use as a flavoring substance and adjuvant is 1.46 mg/p/d, and from its indirect uses is 0.36 mg/p/d. The total EDI of *n*-octanol from its regulated uses is 1.9 mg/p/d. Likewise, the EDI of 1,3-butadiene from the use of *n*-octanol in microcapsules is 0.6 pg/p/d, from the use of *n*-octanol as a flavoring substance and adjuvant is 1.5 ng/p/d, and from the indirect uses of *n*-octanol is 0.35 ng/p/d. The total EDI of 1,3-butadiene from the food use of *n*-octanol is 1.9 ng/p/d. (In our 5-3-94 memorandum, the total EDI of 1,3-butadiene from the use of *n*-octanol was incorrectly reported to be 1.5 ng/p/d.)

To Impurities in *n*-Octanol

Exposure to the four impurities in *n*-octanol can be calculated by multiplying the EDI of *n*-octanol from all its regulated uses (1.9 mg/p/d) by weight percent of each impurity in *n*-octanol. The weight percent of each impurity in *n*-octanol and the EDI of each impurity from the use of *n*-octanol are tabulated below:

¹The poundage data was obtained from the "1987 Poundage and Technical Effects Update of Substances Added to Food," prepared for the Food & Drug Administration by the National Research Council.

<u>Impurity</u>	<u>Weight % in <i>n</i>-Octanol</u>	<u>EDI $\mu\text{g/p/d}$</u>
3-octanol	0.11	2.0
diethyloctylamine	0.10	1.8
dioctylether	< 0.001	< 0.02
2-hexyldecyloctylether	< 0.001	< 0.02

Proposed Regulation

The language of the proposed regulation, with which we concur, is as follows:

21 CFR 172.864 (Synthetic fatty alcohols)

(a)(3) *n*-Octyl; manufactured by the hydro-dimerization of 1,3-butadiene, catalytic hydrogenation of the resulting dienol, and distillation to produce *n*-octanol with a minimum purity of 99.0%.

Summary

Exposures to *n*-octanol prepared by the hydro-dimerization process, its impurities, and the contaminant 1,3-butadiene have been presented. 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 will not be expected to increase as a result of regulation of this petition. We have no questions.



Roseann F. McDaniel, Ph.D.

HFS-226; 245; 248 (Hollifield); 247 (Kuznesof)
HFS-247:RFMcDaniel:254-9537:rfm:4a4419a.pet:7-8-94, 7-25-94
RD Init:MAAdams, 7-26-94

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