DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Memorandum

Date March 7, 1983

From Food Additives Evaluation Branch (HFF-156)

Subject (b) (4) Pentanoic 4,4-bis[gamma, omega-perfluoro-C8-C20-alkyl)thiol] Derived Compounds with Diethanolamine. 21 CFR 176.170

To Dr. John Herrman
Petitions Control Branch (HFF-334)

FOOD ADDITIVE PETITION NO. 3B-3700

CIBA-GEIGY Corporation
Adsley, New York 10502
(AF 20-332)

Name of additive:

(b) (4) A reaction product of 2 moles of 1,1,2,2-tetrahydro-per-fluoro alkyl mercaptans and 1 mole of levulinic acid, as diethanolamine salt.

Chemical Structure:

(b) (4)

CAS # 71608-61-2

$R_FCH_2CH_2S$ > C $CH_2CH_2COO^-$ $H_2N^+(CH_2CH_2OH)$ -CAS # 111-42-2-
$R_FCH_2CH_2S$ |
CH_3

- (b) (4) CAS # 71608-60-1)

Composition of (b) (4)

(b) (4)

Remainder is water

Contains diethanolamine as salt.

(b) (4)

000566

R_F: Perfluoro alkyl group distribution is given as:

R_F		%	Mol. Wt.
C_6F_{13}	-	0-10%	380
C_8F_{17}	-	25-40%	480
$C_{10}F_{21}$	-	35-55%	580
$C_{12}F_{25}$	-	5-20%	680
$C_{14}F_{29}$	-	0-10%	780
$C_{16}F_{33}$	-	0-1%	880
$C_{18}F_3$ or $C_{20}F_{41}$	-	less than 0.1%	

Thus, the basic compound $R_FCH_2CH_2S$ is a complex mixture where R_F varies from C_6F_{13} to $C_{14}F_{29}$. Furthermore the (b) (4) formulations would contain diethanolamine salts, (b) (4)

Inherent impurities in (b) (4) are mentioned as:

Chemical	% in (b) (4)	Anticipated in Paper
Diethanolamine	0.6%	0.09 ppm
Levulinic acid diethanol -amine salt	0.3%	0.05 ppm
Diethanolamine Hydrochloride	0.8%	0.12 ppm
Disulfides:	1.2%	0.023 ppm
$R_FCH_2CH_2S.CH_2CH_2R_F$ (side rxn)		
$R_FCH_2CH_2SH$ Unreacted	0.01%	NONE
Toluene Solvent	.01%	NONE

Use:

As a fluorochemical sizing agent for imparting oil, grease, and water repellency to paper at 8 pounds per ton of paper pulp.

Toxicity data:

Note: Most all acute toxicity data were developed at M.B. Research Laboratories, Inc. Spinner Town, PA 18968. They give an approximate estimate LD_{50} only.

1. Test Material: (b) (4) MB Project # 80-4776A dated 8/21/80

   Acute oral LD_{50} is given as greater than 15 gm/kg. A group of fasting Wistar (5/sex/group) rats about 180-250 gm body weight were intubated with a 50% w/v suspension of compound in Mazola oil. From a two-week observation period, and as per 16 CFR 15003, the compound is classed as "non-toxic".

2. Test Material: (b) (4) salt formulation). MB. project #s 80-4777B, 80-4777C and 80-4777D.

   Acute oral LD_{50} is given as greater than 15 gm/kg for the formulation. The design and conduct of experiment was same as above, based on a single dose estimate.

   Acute dermal LD_{50} is given as greater than 2 gm/kg with rabbits. The material was applied after Draize's method on the abraded, shaven skins of 2 rabbits of each sex for a single application at a single dose level for 24-hour dermal exposure.

   Dermal irritation test (0.5 ml on 2.5 cm. square gauze cloth on shaven abraded skins of 6 rabbits (for 24-hour) and eye irritation test (0.1 ml/eye of 6 rabbits) as per Draize's method classed the formulation to be as "minimal" irritant.

3. 30-days subacute oral with (b) (4) (a dispersion of (b) (4) acid): Toxigenetic lab. report # 410-0387 dated April 6, 1981

Test animals: Sprague-Dawley albino rats in groups of 15/sex about 47 day old with 165-256 gm bodyweight were used.

Dose groups 0 (b) (4), 200, 600 or 1800 mg (b) (4) /kg/day, via gavage.

Duration: 30 days.

With the criteria of toxicity evaluation, namely bodyweight, food consumption, mortality, hematology (CBC), blood chemistry (SGOT, glucose, BUN, alkaline phosphatase, SGPT, LDH and electrolytes), urinalysis, organ weight, organ to body weight data, gross and microscopic pathologies, the report claims no significant harmful effects through the administration of (b) (4) [redacted]

Comment: The duration of experiment is too short to be of value to set any no-effect level for this study. Furthermore, the test material is a complex compound, administered as a dispersion in (b) (4) [redacted]

The above data may be considered adequate if the dietary exposure could remain as "virtually nil, less than 0.05 ppm", and the chemical identity of compound could be specifically defined in the regulation. Chemistry (HFF-458) memo of Feb. 10, 1983 gives a tentative dietary exposure of 0.054 ppm of additive with an EDI of 0.16 mg/person/day.

Evaluation:

The proposed food additive is a complex mixture of several homologous members of fluoro-mercapto chemicals and their diethanolamine salts. A more accurate chemical identity specification should be required than is proposed. Analytical assay data appears to be so crude that it can not define and differentiate chemical entities which could migrate to the packaged food. Similarly, no suggestion is given about the diethanolamine migration as a free entity or as salt of the complex chemical.

If we are to be advised that the only migrant is fluorine (extrapolated) based complex and is "virtually nil" in amount then we will not be able to object to the regulation. However, we would have preferred to have asked for more accurate LD_{50} data profiles on various purer constituent components of RF-based mercaptan acids and their salts, and those at "virtually nil" migration levels.

Conclusion:

We will defer safety appraisal of the proposal, until the Division of Chemistry finalizes its migration and exposure estimates.

[redacted] 3/7/83
Krishna P. Misra, Ph.D.

INIT:MvanGemert MVG 3-8-83

cc: HFF-100
HFF-152
HFF-334
HFF-458

KPMisra:dlm:RD2/24/83:HFF-156:472-5701:Doc#1023A:Arc#0032A:FT3/7/83