8EHQ-0586-0594S Follow-up
PDCN 88-8600069
89-8600043

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6pp

July 23, 1986

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Document Control Officer (TS-790)
ATT: 8(e) Coordinator
Information Management Division
Office of Toxic Substances
U. S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460

RE: 8EHQ-0386-0594S, Octyltin Ester Mixture,
Follow-Up of EPA Requested Information

Dear Madam/Sir:

CIBA-GEIGY Corporation requests that all information shown in brackets in this letter be treated as Confidential Business Information. We enclose a sanitized copy of this letter for the public file.

This is a continued reply to your letter of April 16, 1986, requesting any supplemental information that becomes available. Our most recent reply of May 21, 1986, indicated that we had just received the results of a limited 2-year carcinogenicity study run in France and would have it translated. This letter describes those results as well as results of several other studies of which we have since become aware.

We have carefully reconsidered the extent of our previous confidentiality claims and have determined that release of some of them would cause us no great harm. We have decided, therefore, to relinquish all confidentiality claims relating to: company name, precise chemical identity of the minor component of the mixture, import and sampling volumes, and TK identification number. We do, however, wish to retain confidential, our tradename and percentage of the mixture. To substantiate these latter two claims, we address the relevant six questions for each in Attachment I.

Descriptions of relevant additional studies follow:

1. Limited Carcinogenicity Study; July 10, 1975 (Run in France).
   The test material was Octyltin tris(thioglycolic acid), 2-ethylhexyl ester, CASRN 27107-89-7.

   A limited carcinogenicity study was performed on Wistar rats. One experimental group of animals (20 males & 20 females) were fed diet containing 100 ppm test material. The report concluded that the test material was not carcinogenic at the dose administered.

2. Limited carcinogenicity study; June 9, 1975 (Run in France). The test material was [ ].

A limited carcinogenicity study was performed on Wistar rats. One experimental group of animals (20 males & 20 females) were fed diet containing 100 ppm test material. The report concluded that the test material was not carcinogenic at the dose administered.

3. 10-day oral toxicity study in the rat; October 2, 1976. The test substance was [ ].

The test material was administered orally once a day for ten consecutive days to rats by gavage. The dose groups were 0, 20, 60 and 200 ul/kg/da, and each group was comprised of 5 males and 5 females. Highlights of the major findings are discussed below:

The NOEL for body weight alterations and symptomatology findings was 20 ul/kg. At 200 ul/kg, body weight loss was noted and various symptoms of systemic toxicity were noted; e.g., muscular hypotonicity, irregular breathing, stiff gait and Straub's tail. Two females died in the 60 and 200 ul/kg groups.

Various lab tests were altered in the 200 ul/kg group. There were decreases in blood glucose, serum alkaline phosphatase and serum protein. Increases were observed in blood urea nitrogen, hemoglobin, hematocrit levels (with a normal red cell count) and total leukocytes (as a result of incipient neutrophilia).

Elevated serum alkaline phosphatase was the only alteration in the lab tests for the 20 and 60 ul/kg groups.

The liver, adrenal glands, spleen and thymus weights were decreased and all these organs had histopathological alterations at the 200 ul/kg level. All high dose animals displayed lipoid depletion of adrenal glands, atrophy of lymphatic tissues of the spleen, slight atrophy of the liver cells and moderate to severe thymocyte depletion of the thymus. The 20 ul/kg group was the NOEL for histopathological alterations.

4. TNO subchronic (90-day) toxicity studies with two organic tin compounds in albino rats; January, 1970. The compositions of the test materials were as follows:

		Sample 1	Sample 2
1)	Octyltin tris(thioglycolic acid), 2-ethylhexyl ester, CASRN 27107-89-7	[ ]	[ ]
2)	Dioctyltin bis(thioglycolic acid), 2-ethylhexyl ester, CASRN 15571-58-1	[ ]	[ ]
3)	Trioctyltin (thioglycolic acid), 2-ethylhexyl ester, CASRN 61912-55-8	[ ]	[ ]

These percentages were determined on the basis of the starting materials, not by direct analysis.

The test materials were administered to rats for 90-days at levels of 0, 10, 25, 50, 100, 250, 500 or 1000 ppm in stock diet. The primary findings centered on alterations of the thymus, kidney, liver and, to a lesser extent hematological parameters.

Associated with increased mortality and decreased growth rate were slight decrease in hemoglobin content and white blood cell counts at dietary levels of 250 and 500 ppm. There was a shift in the differential white blood cell counts with an increased number of neutrophiles and decreased lymphocytes at dietary levels of 100 ppm or more.

Varying degrees of renal and hepatic alterations were seen in the high dose levels. The changes included microscopic alterations (swollen epithelium, increased numbers of disintegrated, disquamated tubular cells), decreased urine specific gravity and increased UGOT. The hepatic changes involved minor treatment-related histopathological changes (homogeneous cytoplasm, variation in nuclear size and chromatin pattern, slight proliferation of "oval" cells and isolated cell necrosis), increase in SAP and increased organ weight.

The primary effects on the thymus included decreased organ weight and the following treatment related pathological changes:

a) The thymus of some animals were almost completely devoid of lymphocytes (thymocytes) and the remaining thymic parenchyma, which consisted of reticular cells, hardly permitted a distinction between cortical and medullary regions.

b) A diminished activity in other lymphoid organs (lack of "germinal centers" and depletion of splenic lymphocytes) occasionally occurred.

5. Certain acute handling safety studies for [ ] were cited in the Material Safety Data Sheet (MSDS) sent to EPA with our letter of May 21, 1986. These results may be summarized as follows:

a) Acute oral LD_{50}, rats; May 8, 1986: 3050 (2340-3960) mg/kg

b) Skin irritation, rabbits; April 15, 1981: Slight, Draize score 1.9/8

c) Eye irritation, rabbits; April 16, 1981: Minimal, Draize score 2/110 at 72 hours, not rinsed

d) Ames test; August 26, 1979: Negative

e) Ames test; September 15, 1983: Positive in strain TA 100 without activation

Very truly yours,

CIBA-GEIGY Corporation

A. Di Battista

A. Di Battista
Manager, Toxic Substances Compliance
Safety, Health & Ecology

ADIB1:3:mc
Attachment 1

ATTACHMENT I

SUBSTANTIATION OF CONFIDENTIALITY CLAIMS FOR 8EHQ-0386-0594S, OCTYLTIN ESTER MIXTURE

A. For confidentiality of tradename, the answers to EPA's questions are:

1. Confidential treatment of tradename should be maintained indefinitely.

2,3,5. Tradename is obviously not maintained confidential; however, the linkage with the precise chemical composition has never been released to non-CIBA-GEIGY personnel, except under secrecy agreements, if at all. Product safety related documents and product literature refer only to a generic identity. Precise chemical composition information for this product is confidential information available only to product safety, product management, and relevant marketing personnel on a need to know basis. Such file information is marked "Confidential" and kept within the offices of those having regulatory responsibility for the product. While this product is not sold in the U.S., our affiliated company in Europe does actively sell the product. If the EPA and the tradepress published the tradename together with the precise chemical identity, it is obvious that competitors in Europe would immediately learn the composition of this product. They could then freely produce similar products and potentially capture a share of our affiliated company's market without expending any development effort. For these organotin stabilizers, the composition and ratio of the components are very important in determining the effectiveness of the product, with only modest changes causing significant performance changes. Optimum compositons have been developed only by expending considerable research and development money and time. Competitors could develop a similar product without such development efforts if the precise chemical identity of this product is linked with its tradename.

4. There have been no such confidentiality determinations.

6. This information was voluntarily given as defined in 40 CFR 2.201(i). Obviously, if the tradename is made public in this case, causing us the harm cited above, we would in future be much less inclined to disclose to EPA tradenames associated with 8(e) notifications.

B. For percentages of a mixture, the answers to EPA's questions are:

1. Confidential treatment of percentages of the mixture should be maintained indefinitely.

2. Any documents containing composition information, including percentage of each component, are marked "Confidential" and treated accordingly. Such documents are maintained in product safety and product management files and under the control of the relevant responsible person. Such information is not made known to others inside CIBA-GEIGY except on a need-to-know basis and has not been made known to others outside CIBA-GEIGY. Such information is not disclosed in product safety related documents or product literature.

3. As stated above, only those CIBA-GEIGY personnel having a need to know this information have access to it. They are under strict guidelines to not release it to others, especially others outside CIBA-GEIGY without express permission of the relevant product manager.

4. There have been no such determinations.

5. The crucial determinants of the performance of an organotin stabilizer are precise chemical compositon and component ratios. We have already given up the chemical composition. To now release the percentages of the mixture information would allow competitors to produce an identical product and assail the markets of our affiliated company outside the U.S. It is conceivable that these competitors could sell such a product at a lower price than ours because they would not have to amortize extensive research and development costs.

   Confidentiality of the precise composition of proprietary product mixtures is crucial and should be protected. The importance of keeping such information confidential has been embodied by Congress in Section 14(b) of TSCA.

6. We do not assert that such information was given voluntarily as defined in 40 CFR 2.201(i). It appears that precise chemical composition must be given to EPA for TSCA Section 8(e) submissions, when such information is known.

ADIB1:4(3):mc