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July 2, 2004

Dockets Management Branch
Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20857

Re: Docket # 03N-0233

Dear Madam or sir:

On July 11, 2003, FDA issued a Federal Register notice requesting the submission of data supportive of the safety and effectiveness of octyl triazone.^{1/} BASF AG of Ludwigshafen, Germany responded to this notice on October 3, 2003 and submitted a document containing twenty-five attachments as demonstration of the safety and effectiveness of octyl triazone as an active sunscreen ingredient.

Following the submission of this data, you requested that we clarify whether BASF intended to maintain as confidential specific sections in the submission which were marked as confidential.

^{1/} See 68 Fed. Reg. 41386 (July 11, 2003).

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Food and Drug Administration

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This letter is intended to confirm that BASF does not intend to treat as confidential the safety and efficacy studies contained in this submission. Accordingly, all references to confidentiality have been removed from these materials. In addition to the issue of confidentiality, several of the studies were missing pages, and these have been added. Consequently, included are amended copies of the original submission. Please note that although only Attachments 2-18 were revised, we have included full copies of the of the amended submission (i.e., Attachments 1-23).

Sincerely,



Kathleen M. Sanzo

Attachments 1-23

c: Matthew Holman, CDER
Michael Koenig, CDER

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October 3, 2003

BY HAND

Docket No. 03N-0233

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

Dear Madam or Sir:

Pursuant to the notice published in the Federal Register on July 11, 2003¹, BASF AG of Ludwigshafen, Germany respectfully submits these data as demonstration of the safety and effectiveness of the sunscreen ingredient, octyl triazone.² BASF AG has marketed octyl triazone under the trade name Uvinul T 150, and previously under the name Lusantan T3, as an active sunscreen ingredient since at least 1988. Based on the sum of the data provided in this submission and the substantial marketing history³ of octyl triazone as a safe and effective product in Europe and elsewhere, BASF AG requests that octyl triazone be determined to be generally recognized as safe and effective ("GRAS/E") drug and included as an active ingredient in the Agency's monograph for OTC sunscreen drug products, 21 C.F.R. § 352.10. In accordance with current FDA regulations,⁴ confidential data contained in this submission is appropriately marked and is not intended for public release.

¹ See 68 Fed. Reg. 41386 (July 11, 2003).

² 2,4,6-trianilino-p-(carbo-2-ethylhexyl-1-oxi)-1,3,5-triazine, CAS No. 88122-99-0. See Attachment 1 for the structure of octyl triazone.

³ See Time and Extent Application (TEA) for octyl triazone, Docket No. 96N-0277 (Aug. 21, 2002), filed on behalf of BASF AG by Kathleen M. Sanzo, Esq. Morgan, Lewis & Bockius LLP.

⁴ See 21 C.F.R. § 310.14(f)

Data and Information Supporting the Safety of Uvinul T 150

Uvinul T 150 is generally recognized by qualified experts to be safe as a sunscreen active ingredient based on the following data and information, which are contained in attachments 2-23.

- a) The LD50 for oral doses of Uvinul T 150 in the rat is greater than 5,000 mg/kg (Attachment 2).
- b) The LD50 for dermal doses of Uvinul T 150 in the rat is greater than 5000 mg/kg (Attachment 3).
- c) Uvinul T 150 tested negative as a skin or mucous membrane (eye) irritant to the white rabbit (Attachment 4 and 5).
- d) The substance was found not to be an irritant in the HET CAM chicken embryo toxicity test (Attachment 6).
- e) In a sensitization maximization test of 40 % Uvinul T 150 in olive oil in the guinea pig, the substance was found to be non-sensitizing (Attachment 7).
- f) The substance was found to produce no phototoxic or photoallergenic reaction in the guinea pig (Attachment 8).
- g) A four-week dermal irritation study of 50 % Uvinul T 150 in polyethylene glycol found no irritating or sensitizing effects (Attachment 9).
- h) Human skin irritation studies using the product as 5 and 10 % emulsions in oil and as 5% in glyceryltri octanoate and as 3% in skin cream found no irritating or sensitizing effects (Attachment 10).
- i) Uvinul T 150 tested negative as a mutagen in the Ames test (Attachment 11).
- j) Micronucleus testing of Uvinul T 150 in mice at doses of 525, 1050 and 2100 mg/kg found no chromosome damaging or chromosome distribution impairing effects (Attachment 12).
- k) In vitro chromosome aberration assays found no mutagenic effect from Uvinul T 150 (Attachment 13).
- l) Photomutagenicity/gene mutation assays in E. coli and mammalian cells found no photomutagenic effect from Uvinul T 150 (Attachment 14 and 15).

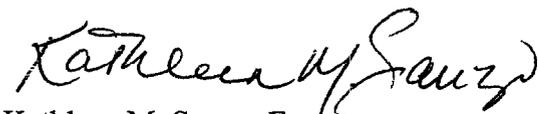
- m) Skin penetration tests found 0.5 and 1.5% penetration rates after twenty-four hours (Attachment 16).
- n) In three month oral toxicity studies in the rat at concentrations of Uvinul T 150 of 1000, 4000, and 16,000 ppm, no toxicity was detected (Attachment 17).
- o) No teratogenic potential was found in the rat when administered at 100, 400 and 1000 mg/kg body weight/day (Attachment 18).
- p) BASF AG has not received and is not otherwise aware of any reported adverse reactions directly attributable to the ingredient during its long period of use.
- q) Uvinul T 150 has been approved for marketing in the EU as a sunscreen ingredient since the 11th Commission Directive (89/174EC) of 21 February 1989 (see Attachment 19).
- r) Uvinul T 150 was approved for use in Japan in March 1996 (see Attachment 20).

Data Supporting the Efficacy of Uvinul T 150

Uvinul T 150 is generally recognized by qualified experts to be effective as a sunscreen active ingredient. Numerous studies have shown the efficacy of Uvinul T 150 using the DIN SPPF testing protocol. See Attachment 21; see also Attachment 22 (comparing FDA and DIN protocols for SPF testing). In addition, the substantial photostability of Uvinul T 150 has been demonstrated. See Attachment 23. These data confirm the effectiveness of this product, which has a long marketing history in a number of countries outside the U.S.^{5/}

Based on these data and the substantial history of safe and longstanding use of Uvinul T 150 in other countries, BASF AG requests that octyl triazone be considered GRAS/E and included as an active ingredient in the Agency's monograph for OTC sunscreen products, 21 C.F.R. § 352.10.

Sincerely,



Kathleen M. Sanzo, Esq.
Counsel to BASF AG

Attachments 1-23

^{5/} See TEA filed by BASF AG, supra n.4.