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Submitting Organization		CONFIDENTIAL			
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Document Title		INITIAL SUBMISSION: LETTER FROM [] TO USEPA RE: 28-DAY DIETARY TOXICITY STUDY IN ALBINO RATS AND 28-DAY DIETARY TOXICITY STUDY IN ALBINO MICE WITH [], DATED 07/08/99 (SANITIZED)			
Chemical Category		CONFIDENTIAL			

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Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street S.W.
Washington, DC 20460

8EHQ-99-14510
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Attention: Section 8(e) Coordinator

Dear Sir/Madam:

The purpose of this letter is to inform you, under TSCA Section 8(e), of results of two toxicity studies; 28-Day Dietary Toxicity Study in Albino Rats and 28-Day Dietary Toxicity Study in Albino Mice. The research materials are identified as:

XXXXXXXXX designated as XXXXXXXXXXXXXXXXXXXXXXXXXX designated generically as a substituted aroyl ester.

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Compound Structure: XXX

28-Day Dietary Toxicity Study in Albino Rats (Study T-1091)

The study was conducted at dietary concentrations of 0, 1000, 5000, 10,000 and 20,000 ppm for a period of 28-days. Food consumption, mean body weights and weight gains were reduced for both sexes at 20,000 and 10,000 ppm and in females at 5000 ppm, as compared to controls. No effects on weight gain or food consumption were observed at 1000 ppm. No hematological effects were observed in either sex at any dose level. Blood urea nitrogen (BUN) levels at termination were increased in both sexes at 20,000 and 10,000 ppm and in females at 5000 ppm. A slight increase in absolute and relative (to body weight) liver weights were observed for both sexes at all dose levels. At necropsy, yellow calculi were observed in the bladders and kidneys of both sexes at 5000, 10,000 and 20,000 ppm. Additionally, the kidneys were soft and hollow at doses of 5000 ppm and above. Histopathological findings correlating with the observed increases in BUN and gross pathology were observed in the kidneys at all dose levels. Specifically, increased incidences of tubular nephrosis [20,000 ppm (9/10), 10,000 ppm (9/10), 5000 ppm (4/10), 1000 ppm (0/10)] and regenerative tubular epithelium [20,000 ppm (9/10), 10,000 ppm (10/10), 5000 ppm (7/10), 1000 ppm (8/10), Control (3/10)]. Based on the presence of tubular nephrosis observed at 5000 ppm, the NOAEL for the study is 1000 ppm (approximately 110 mg/kg b.w./day, estimated from food consumption data).

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28-Day Dietary Toxicity Study in Albino Mice (Study T-1097)

The study was conducted at dietary concentrations of 0, 1000, 3500 and 7000 ppm for a period of 28-days. Food consumption, mean body weights and weight gains were reduced for both sexes at 7000 ppm and in females at 3500 ppm, as compared to controls. No effects on weight gain or food consumption were observed at 1000 ppm. Hematological and clinical chemistry evaluations done at termination showed statistically significant increases in AST, ALT, GGT, Alkaline phosphatase, and cholesterol at the 7000 ppm and 3500 ppm doses in both males and females. Increases in these enzymes are indicative of severe liver damage. Additionally, RBC counts, hemoglobin and hematocrit values were statistically significantly reduced in males and females at the 7000 ppm and 3500 ppm doses indicating a possible anemic condition. These same clinical

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chemistry parameters for 1000 ppm males and females were also slightly increased but were not statistically significant. At necropsy, absolute and relative liver and spleen weights were statistically significantly increased in both sexes at all treatment levels. Calculi were observed in the urinary bladder of one male at the 7000 ppm dose only. No evidence of kidney degeneration was evident at any of the treated animals. Histopathological evaluation of tissues from animals at the 7000 ppm, 3500 and 1000 ppm concentrations confirmed the presence of liver damage as evidenced by the presence of multifocal liver necrosis in 10 of 10 mice at the 7000 and 3500 ppm concentrations and 7 of 10 mice at the 1000 ppm concentration. Additionally, extramedullary hematopoiesis was observed in the spleens of both sexes at the 7000 (9 of 10) and 3500 ppm (10 of 10) concentrations and in 4 of 10 females at the 1000 ppm concentration, confirming the anemic state of the animals.

We are currently evaluating the significance of these results. This material is under research and development and is not distributed in commerce.

If further information is required, please contact J.M. Provenzano-Gray, Regulatory Compliance Manager at 609-716-2780.

Sincerely,



L.R. Miko

Vice President Global Quality Assurance & Information Technology

Support Information for Confidentiality Claims

TSCA 8(e) Submission on

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1. For what period of time do you assert this claim of confidentiality? Explain why the information should remain confidential until such event or time.

Confidentiality is claimed for a period of 10 years from the date of this submission pending finalization of the application for a patent on the test material and the process for its synthesis. It is suggested that the generic name substituted aroyl ester be used in reference to this 8(e) submission. The period between the synthesis of a research chemical and full determination of its uses is often quite long. It is important for an R&D organization to protect the confidentiality of its key resource library of chemicals.

2. Have there been any confidentiality determinations made by the EPA, other Federal agencies or courts in connection with this information?

No.

3. Has any of the information that you are claiming as confidential been disclosed to individuals outside your company? Will it be disclosed to such persons in the future? If so, what restrictions, if any, apply to use or further disclosure of the information.

Information regarding the name and structure have not been disclosed to persons outside the employ of the company. Until such time as patents are issued for the structure and the processes for synthesis of the material we do not plan to disclose such information to persons outside the company who would not be under an agreement of confidentiality regarding such information. Such persons would include laboratory or field personnel conducting studies with this material under contract to the company or expert consultants we may retain. Other persons outside the company will become informed after the above referred patents are obtained and our evaluation of the material is complete.

4. Briefly describe any physical or procedural restrictions within the company relating to the use and storage of the information you are claiming confidential. What other steps, if any, have you taken to prevent undesired disclosure of the information during its use or when an employee leaves the company.

The information has been given to only those individuals with a need to know. The information is considered "company confidential" and all employees who have access to this information are required to keep it confidential. Employees who have access to this information have signed confidentiality statements with regard to any such proprietary information.

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5. Does the information claimed as confidential appear or is it referred to in any of the items listed below?

- advertising or promotional materials for the chemical or the end product containing it ;
- safety data sheets or other such materials for the chemical or the end product containing it;
- professional or trade publications;
- any other media available to the public or to your competitors:

If you answered yes to any of the above questions, you must indicate where the information appears and explain why it should, nonetheless, be treated as confidential.

No

The information that is to be held confidential about the chemical name may appear in a Material Safety Data Sheet prepared by the company for distribution to company personnel and contracted cooperators who are involved in the technical evaluation of the material in various field trials. Such persons will have signed confidentiality agreements.

6. Would disclosure of this information be likely to result in substantial harm to your competitive position?

Disclosure of this information, prior to issue of the patents for the material and the processes for synthesis would jeopardize the proprietary nature of the material and would potentially cause the company to lose the advantage currently available though the fact that this information is not available to the competition in this market. The company is synthesizing and filing patents on analogs of this chemistry. Release of the information requested to be held confidential would aid competitive companies in analog synthesis. The technical attributes are still under investigation for this compound and the analogs, which may possess more favorable biological characteristics. Additional use patents have also not yet been filed. Disclosure could also jeopardize our patent positions in foreign countries. Although patent protection is guaranteed in the U.S. by FIFRA, there is no guarantee of protection in other countries. Further, misinterpretation or misrepresentation of these preliminary data could cause undue alarm to our customers and, thereby, damage our potential customer base. The period between the synthesis of a research chemical and full determination of its uses is often quite long. It is important for an R&D chemical organization to protect the confidentiality of its key resource library of chemicals.

The use of this chemistry is directed at terrestrial crops and direct application to water is not contemplated. The potential for exposure of aquatic habitats to this chemistry is low. The use of acute toxicology data deriving from direct exposure of aquatic species is not indicative of true exposure under use and could cause undue alarm when presented out of context.

7. If the information in question is "health and safety data" pursuant to 40 CFR part 2.306 (3) (i), do you assert that disclosure of the information you are claiming confidential would reveal:

- confidential process information;
- confidential portions of a mixture; or
- information unrelated to the effects of the substance on human health or the environment ?

Aside from the chemical structure and names this submission does not reveal any information related to the process, product composition or other information unrelated to human health effects or the environment.