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Chemical Category			Acetyl ferrocene		

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Original Submission

Document Control Officer  
Information Management Division  
Office of Toxic Substances (TS-793)  
U.S. Environmental Protection Agency  
401 M Street, S.W.  
Washington, D.C. 20460

Dear Sir:

This notice is being submitted to the Administrator of the U.S. Environmental Protection Agency (U.S. EPA) in accordance with section 8 (e) of the Toxic Substances Control Act (TSCA). Preliminary toxicity tests have been completed on laboratory rats and rabbits using the chemical acetyl ferrocene, which is currently being manufactured at one of our Syntex Chemical facilities. These preliminary test results were reported to the Syntex Corporation Toxic Risk Evaluation Committee, which sits in Palo Alto, California. In accordance with our corporate Toxic Risk Evaluation Committee guidelines, the Committee met on this issue and determined that this data may constitute "substantial risk" information under section 8 (e) of TSCA. Furthermore, it was determined that, to the best of the Committee's knowledge, information on the potential of acetyl ferrocene to be highly toxic to animals has not been previously reported to the Administrator.

Acetyl ferrocene has been in use for at least fifteen years at one of our Chemical facilities, with no reported adverse health effects. This chemical is an intermediate in the manufacture of one of our ultimate products, and there is currently no contact between this chemical and the general public. Neither is any such contact contemplated in the future. Acetyl ferrocene was one of many different chemicals recently tested as part of Syntex Corporation's Environmental Health and Safety periodic occupational toxicology testing program.

Preliminary results were obtained from acute oral toxicity, eye irritation and acute dermal toxicity tests performed on laboratory rats and rabbits. Oral toxicity studies were initially conducted on groups of two male and two female rats at doses of 50, 150 and 500 mg/kg. All of the animals died within thirteen days after dosing, with most deaths occurring on the second and third days. Toxic signs included inactivity, kyphosis, rough coat, unthriftiness, salivation and ptosis. Female animals appeared to be more sensitive than males. This preliminary data suggested that the oral LD50 for acetyl ferrocene in rats was less than 50 mg/kg.

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To further confirm and define the oral toxicity of acetyl ferrocene, the oral toxicity testing was repeated on two groups of five male and five female rats. One group was administered one dose at 50 mg/kg, and the second group was given 5 mg/kg. All the females in both groups died within four days. All of the male rats given low doses survived, but only one male rat survived at the high dose. A sexual difference in sensitivity was again observed. The oral LD50 of acetyl ferrocene for female rats appears to be less than 5 mg/kg, while the comparable LD50 for males seems to be between 5 mg/kg and 50 mg/kg.

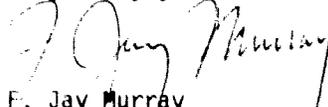
Eye irritation tests were then performed on three female rabbits. Doses of 30 mg/kg (100 mg/rabbit) were administered to each rabbit in the conjunctival sac of the eye. All of the rabbits died on the second or third days following dosing.

Acute dermal toxicity tests were then conducted on groups comprising two male and two female rats, at doses of 50, 500 and 2000 mg/kg. Three animals from the high dose group, and one animal from the medium dose group died on the second and third days, respectively, following dosing. The dermal LD50 in rats appears to be between 50 and 500 mg/kg.

The results of the toxicity testing appear to indicate that while acetyl ferrocene is extremely toxic to laboratory animals in general, the absence of any reported adverse health effects among our employees suggests that there may be important differences in sensitivity to this chemical between humans and animals. We are exploring the possibility of performing additional testing to further interpret the toxic potential of this chemical.

As a result of the preliminary test results, we have reviewed our current personal protective equipment requirements and have made appropriate modifications. In addition, we have updated our Material Safety Data Sheet on acetyl ferrocene and have already distributed this information to pertinent employees. We will keep you informed as to any further developments in this area.

Very truly yours,



F. Jay Murray  
Chairperson,  
Toxic Risk Evaluation Committee

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