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October 9, 1998

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Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M Street, SW
Washington, D.C. 20460
Attn: 8(e) Coordinator

COMPANY SANITIZED

Re: A Series of Research Compounds which may be referred to generically as
Halogenated Alkoxy Substituted Pyrazols:

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Dear 8(e) Coordinator:

hereby submits the following information under Section 8(e) of the Toxic Substance Control Act. While the submitter does not necessarily believe the information indicates a significant risk of injury to health or the environment, EPA guidance seems to indicate that these effects in laboratory animals should be reported to the Agency.

These test substances were evaluated for effects on trigeminal nerves, serum tyrosine, and liver weights. A positive control group was given a structurally similar compound with known effects on trigeminal nerves and serum tyrosine. An additional control group was given untreated rodent chow for 1 year.

U.S. Environmental Protection Agency
Attn: 8(e) Coordinator
October 9, 1998
Page 2

Histopathologic examinations of the right and left trigeminal nerves were performed on all rats by a veterinary pathologist (Diplomate, American College of Veterinary Pathologists).

A treatment-related, statistically identified alteration was noted in the trigeminal nerves of rats given the positive control, Test Substance 2, Test Substance 3 or Test Substance 4 at doses of 1 or 10 mg/kg bw/day; and in rats given Test Substance 1 or Test Substance 5 at a dose of 10 mg/kg bw/day. The treatment-related alteration of individual nerve fibers appears to represent an exacerbation of a spontaneous alteration, as evidenced by the presence of very slight or slight degeneration at the same site of the trigeminal nerve in males from the control group.

The alteration was characterized as degeneration of individual nerve fibers in the motor root of the trigeminal nerve, at a site that consistently involved only the first few millimeters of the root, distal from the transition of oligodendrocytes to Schwann cells. Affected nerve fibers were vacuolated and occasionally accompanied by the accumulation of macrophages. The vacuoles appeared to be within the myelin and tended to separate the axons from most of the myelin. The vacuoles were unilocular or multilocular, and generally ranged from 20 to 200 microns in diameter. Axons were intact in the center of some vacuoles, while axons in other vacuoles were displaced from the plane of section.

There were statistically identified increases in serum tyrosine for all test substances and the positive control.

Liver weights were statistically identified as increased in rats given the positive control, Test Substance 1 or Test Substance 2 at doses of 1 or 10 mg/kg bw/day; and in rats given Test Substance 3, and Test Substance 4 at the dose of 10 mg/kg bw/day.

No Chemical Abstract Registry Numbers are currently available for these substances.

Sincerely,