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E. I. du Pont de Nemours and Company
Haskell Laboratory for Toxicology and Industrial Medicine

HASKELL LABORATORY REPORT NO. 160-69 [redacted]

Material Tested: Ammonium Perfluorooctanoate

Material Submitted by: [redacted] Plastics Department
Washington Plant, Parkersburg, West Virginia

Haskell No.: 6001

Other Codes: [redacted]

ACUTE INHALATION DUST TOXICITY

Procedure: Two different types of dust generators were used to generate ammonium perfluorooctanoate [redacted] aerosols.

(1) DeVilbis Dust Generator: A heavy dust cloud was generated by blowing ~ 30 L/minute of air through a high velocity Cu-tubing jet submerged in a mechanically stirred reservoir of the test material. The air carried the dust particles into an 8-liter exposure chamber. Suitable diluting air was introduced between the generator and the chamber to achieve lower concentrations. This generator did not fractionate the dust and all particle sizes, large and small, were delivered into the exposure chamber.

(2) Hornberger Dust Generator: This generator was used for low atmospheric dust concentrations. With this generator, a falling stream of dust particles from a stirred reservoir impinged on a pneumatic jet. The air stream from this jet carried the particles to a cyclone head where the larger ones were returned to the reservoir. This generator achieved some particle size fractionation and the rats received mainly particles $\leq 5\ \mu$ mass median diameter. As with the DeVilbis generator, the generator itself was run under constant conditions and dust concentrations were lowered by diluting the stream with air between the generator and the exposure chamber.

Six rats of 250-270 grams body weight were used per exposure. Only their heads were exposed. All exposures were four hours. The eyes were stained with fluoroscein immediately after exposure to check on eye damage by the test material. Rats were sacrificed for histopathologic examination at 1, 7, 14, 27, and 42 days post-exposure. Tissues from two rats dying during exposure were also examined microscopically.

In both methods, the airborne solids were measured in the exposure chamber by collecting the solids in a known air volume on a filter of known pore size. The concentration was determined five times during each four-hour exposure. At the mid-point of each exposure, a particle size distribution measurement was made with a Monsanto Cascade Impactor.

Results:

Generat :	Average Dust Concentration (mg/L)	Mortality Ratio	Mass Median Diameter (μ)	Clinical Observations	
				During Exposure	Post-Exposure
1	5.7	6/6	6.4 ± 3.2	Gasping, irregular breathing, red discharge around eyes and nose, salivation, death (1/6)	Death from 15 minutes to 48 hours (5/6)
	4.8	6/6	16 ± 3.4	Same as above, but no deaths	Some rupture of eyes, all other eyes opaque; all dead in 48 hours
	2.2†	6/6	7.6 ± 3.8	Same as above	Same as above; fluorescein stain confirmed external eye damage
2	0.83‡	1/6	1.8 ± 2.5	Gasping, irregular breathing, red discharge around eyes and nose	Severe weight loss first day, mild loss the next day; normal growth thereafter; > 80% of rats have opaque and corroded appearing eyes; external damage confirmed with fluorescein stain; one death 2nd night
	0.81‡	2/6	1.8 ± 2.8	Same as above except one death	Same as above; eyes appeared normal after 20 days
	0.38	1/6§	2.4 ± 2.4	Same as above	Severe weight losses f[illegible]st day; normal growth thereafte[illegible]

† Whole body control exposure.

‡ Sacrificed at 1, 7 and 14 days.

‡ Sacrificed at 27 and 42 days.

§ Death not related to test material.

Pathology: Rats dying during exposure had hyperinflated lungs. Some of the test material was present in the stomach. They also had a foamy white exudate in the trachea. The ratio of liver weight to body weight was at the high end of the normal range one day after exposure. It increased to a maximum (two times normal) at 7-14 days after exposure and then decreased to the high end of the normal range at the last sacrifice, 42 days post-exposure.

Pathology (Cont'd.):

Microscopic tissue examination* indicated that acute pulmonary edema developed promptly but disappeared in about a week, leaving no residual injury. No dust particles were seen in the lungs microscopically. There was irritation of the stomach which cleared in two weeks and irritation of the eyes which was still present when the last pair of rats was sacrificed 42 days after exposure. The liver tissue appeared microscopically normal at all times and the mechanism of enlargement was not apparent.

Discussion: The time pattern and magnitude of rat liver enlargement caused by inhalation of [redacted] were similar to those [redacted]. Inhalation of [redacted] caused changes in liver cell morphology [redacted] but inhalation of [redacted] did not. However, the exposures to the two materials were not strictly comparable, since exposure to [redacted] was whole body, whereas exposure to [redacted] was head only. Thus effects from the [redacted] exposures would reflect ingestion of greater amounts of material from grooming. No strict pattern comparison can be made for liver enlargement caused by inhalation of [redacted] versus ingestion since comparable recovery studies have not been carried out after ingestion of [redacted]. However, 14 days after inhalation of a fractionally lethal dose of [redacted] liver to body weight ratio was two times normal. Fourteen days after ingestion of the highest sublethal oral dose, liver to body weight ratio was < 1.5 times normal [redacted].

A study of rat liver enlargement versus time after ingestion has been carried out for the [redacted]. In this study, the ratio of liver weight to body weight reached a maximum 5-10 days after ingestion of 1/5 of the Approximate Lethal Dose (ALD; dose was 12 mg/kg) and stayed relatively constant for the rest of the study (last sacrifice 56 days after treatment).

[redacted] would be considered highly toxic by inhalation administration as judged by four-hour rat inhalation. Orally, it would be considered to have only moderate acute toxicity.

Summary: The Approximate Lethal Concentration (ALC) of ammonium perfluorooctanoate is 0.8 mg/L for a four-hour rat exposure. It is considered highly toxic by inhalation. Only the rat heads were exposed to minimize complicating the study by ingesting the test material. Inhalation of the test material caused liver enlargement which reached a maximum (two times normal) 7-14 days after exposure. Liver weights returned to the normal range 42 days after exposure. No changes in liver cell morphology were observed. The small amount ingested caused irritation of the stomach which repaired normally. The material also caused corneal opacity and ulceration which were still microscopically evident 42 days after exposure.

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* Lungs, liver, trachea, gastrointestinal tract were the only tissues examined microscopically.

Summary (Cont'd.):

[redacted] should be handled with at least the same care as [redacted] Ingestion and inhalation should be avoided and any spilled on the skin or eyes should be washed off immediately. There should be medical follow-up of any known eye contact.

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