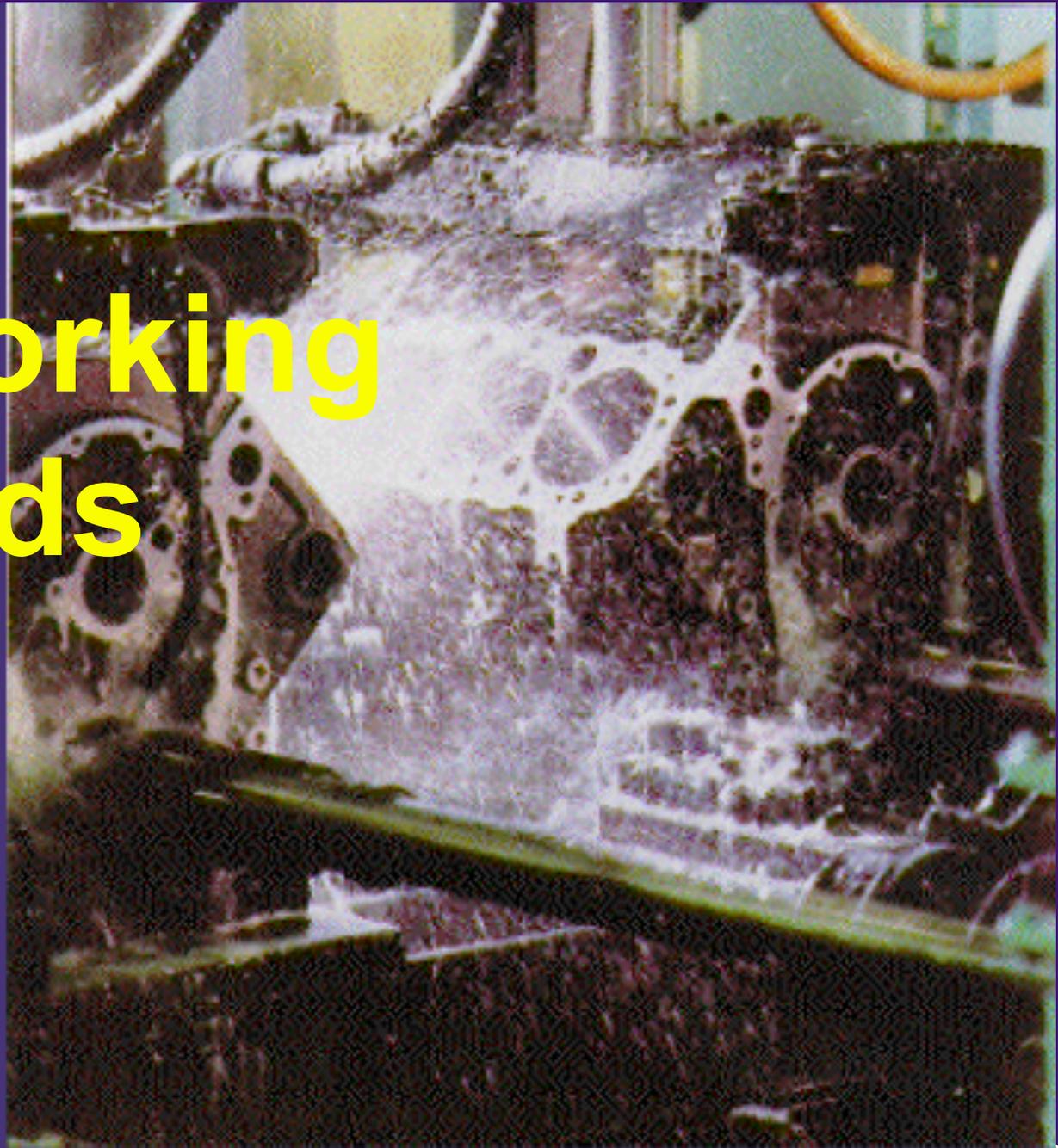


Comments on Technical Report Cimstar 3800

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Metalworking Fluids



History of the Project

- **UAW petition to NTP for bioassay of respiratory effects and carcinogenicity of representative MWF's**
- **Respiratory effects as important to public health as carcinogenic effect**
- **Virgin fluids vs. in use contamination**
- **Composition also very important to apply to various mixtures**

Presentation of Respiratory Pathology

- Report should note near 100% upper respiratory effects at lowest dose tested for 90-day study, 2-year study in rats
- Adjusted incidence should be calculated for non-tumor pathology so that results can be included in benchmark dose analysis
- Only NTP can do this

TABLE 3

**Incidences of Nonneoplastic Lesions of the Respiratory System in F344/NTac Rats
in the 3-Month Inhalation Study of CIMSTAR 3800**

	Chamber Control	25 mg/m ³	50 mg/m ³	100 mg/m ³	200 mg/m ³	400 mg/m ³
Female						
Nose	10	10	10	10	10	10
Goblet Cell, Hyperplasia	0	8** (1.5)	10** (1.5)	9** (1.6)	10** (1.7)	10** (1.8)
Olfactory Epithelium, Accumulation, Hyaline Droplet	0	10** (2.8)	10** (3.0)	10** (2.9)	10** (3.0)	10** (3.0)
Olfactory Epithelium, Inflammation, Suppurative	0	9** (1.0)	10** (1.1)	10** (1.3)	10** (1.6)	10** (1.4)
Respiratory Epithelium, Accumulation, Hyaline Droplet	0	10** (2.6)	10** (2.8)	10** (2.6)	10** (2.8)	10** (2.7)
Respiratory Epithelium, Inflammation, Suppurative	0	9** (1.0)	10** (1.1)	10** (1.3)	10** (1.6)	10** (1.4)
Respiratory Epithelium, Metaplasia, Squamous	0	0	0	0	0	1 (1.0)
Larynx	10	10	10	10	10	10
Inflammation, Chronic Active	0	10** (1.0)	10** (1.1)	10** (1.6)	10** (1.7)	10** (2.2)
Metaplasia, Squamous	0	10** (2.9)	10** (3.4)	10** (4.0)	10** (4.0)	10** (4.0)
Squamous Epithelium, Hyperplasia	0	9** (1.1)	7** (1.0)	10** (1.4)	9** (1.3)	10** (1.7)
Lung	10	10	10	10	10	10
Alveolus, Infiltration Cellular, Histiocyte	0	0	0	0	10** (1.0)	10** (1.0)

TABLE 11

**Incidences of Nonneoplastic Lesions of the Respiratory System in Wistar Han Rats
in the 2-Year Inhalation Study of CIMSTAR 3800**

	Chamber Control	10 mg/m ³	30 mg/m ³	100 mg/m ³
Male				
Nose^a	50	50	50	50
Glands, Olfactory Epithelium, Hyperplasia ^b	1 (1.0) ^c	39** (1.5)	47** (2.0)	50** (2.6)
Goblet Cell, Hyperplasia	0	20** (1.1)	25** (1.1)	34** (1.3)
Olfactory Epithelium, Accumulation, Hyaline Droplet	19 (1.6)	50** (2.8)	50** (3.0)	50** (3.5)
Respiratory Epithelium, Accumulation, Hyaline Droplet	0	17** (1.1)	25** (1.1)	29** (1.2)
Larynx	50	50	50	50
Metaplasia, Squamous	1 (2.0)	47** (1.5)	50** (2.2)	50** (2.7)
Lung	50	50	50	50
Alveolar Epithelium, Hyperplasia	4 (1.3)	6 (1.8)	11 (1.9)	13* (2.4)
Bronchus-associated Lymphoid Tissue, Hyperplasia, Lymphohistiocytic Inflammation, Lymphohistiocytic	0 (1.2)	1 (1.0) 14* (1.0)	5* (1.0) 41** (1.1)	19** (2.0) 47** (1.8)
Lymph Node, Bronchial	42	40	37	35
Hyperplasia, Lymphohistiocytic	0	0	10** (1.1)	28** (2.1)
Lymph Node, Mediastinal	46	45	50	49
Hyperplasia, Lymphohistiocytic	0	0	4 (1.5)	29** (2.2)

Lung Tumors in female mice should be “clear” evidence

- Significance in poly-3 test is evidence for increased incidence and exposure response ($p = 0.006$)
- Monotonic increase in adjusted rate: 9%, 11%, 13%, 27%
- Pairwise comparison in high dose significant ($p = 0.21$)

TABLE 18

**Incidences of Neoplasms and Nonneoplastic Lesions of the Respiratory System in Mice
in the 2-Year Inhalation Study of CIMSTAR 3800**

	Chamber Control	10 mg/m ³	30 mg/m ³	100 mg/m ³
Female (continued)				
Lung (continued)				
Alveolar/bronchiolar Adenoma or Carcinoma ^m				
Overall rate	4/50 (8%)	5/50 (10%)	6/50 (12%)	12/50 (24%)
Adjusted rate	8.8%	10.9%	12.8%	27.2%
Terminal rate	4/39 (10%)	5/37 (14%)	4/37 (11%)	9/33 (27%)
First incidence (days)	731 (T)	731 (T)	460	644
Poly-3 test	P=0.006	P=0.505	P=0.391	P=0.021
Alveolar/bronchiolar Carcinoma ^h				
Overall rate ⁱ	4/50 (8%)	1/50 (2%)	4/50 (8%)	8/50 (16%)
Adjusted rate ^j	8.8%	2.2%	8.6%	18.2%
Terminal rate ^k	4/39 (10%)	1/37 (3%)	3/37 (8%)	6/33 (18%)
First incidence (days)	731 (T)	731 (T)	460	644
Poly-3 test ^l	P=0.021	P=0.176N	P=0.627N	P=0.163

Composition should be cleared up

- **Semi-synthetic contains all components of MWF's: oil, detergent, amines**
- **Detergent not mentioned in discussion**
- **Mineral oil not mentioned in analysis**
- **Compare to MSDS ingredients**
- **Include particle size information – MMD of $\sim 1.5 \mu$ - respirable**

MSDS extract

6 HAZARDOUS INGREDIENTS / IDENTITY INFORMATION

These ingredients may contribute to the acute product hazards listed under the Potential Health Effects section. Other substances, not hazardous under the OSHA Hazard Communication Standard, may be present. Further composition information may be available to health professionals as provided in the Standard.

Component	CAS #	Percent
MONOETHANOLAMINE	141-43-5	3 - 7
SEVERELY-HYDROTREATED NAPHTHENIC PETROLEUM DISTILLATES	64742-52-5	1 - 5
TRIETHANOLAMINE	102-71-6	1 - 5
SODIUM ALKYL BENZENE SULFONATE	78330-12-8	1 - 5
MONOISOPROPANOLAMINE	78-96-6	1 - 5