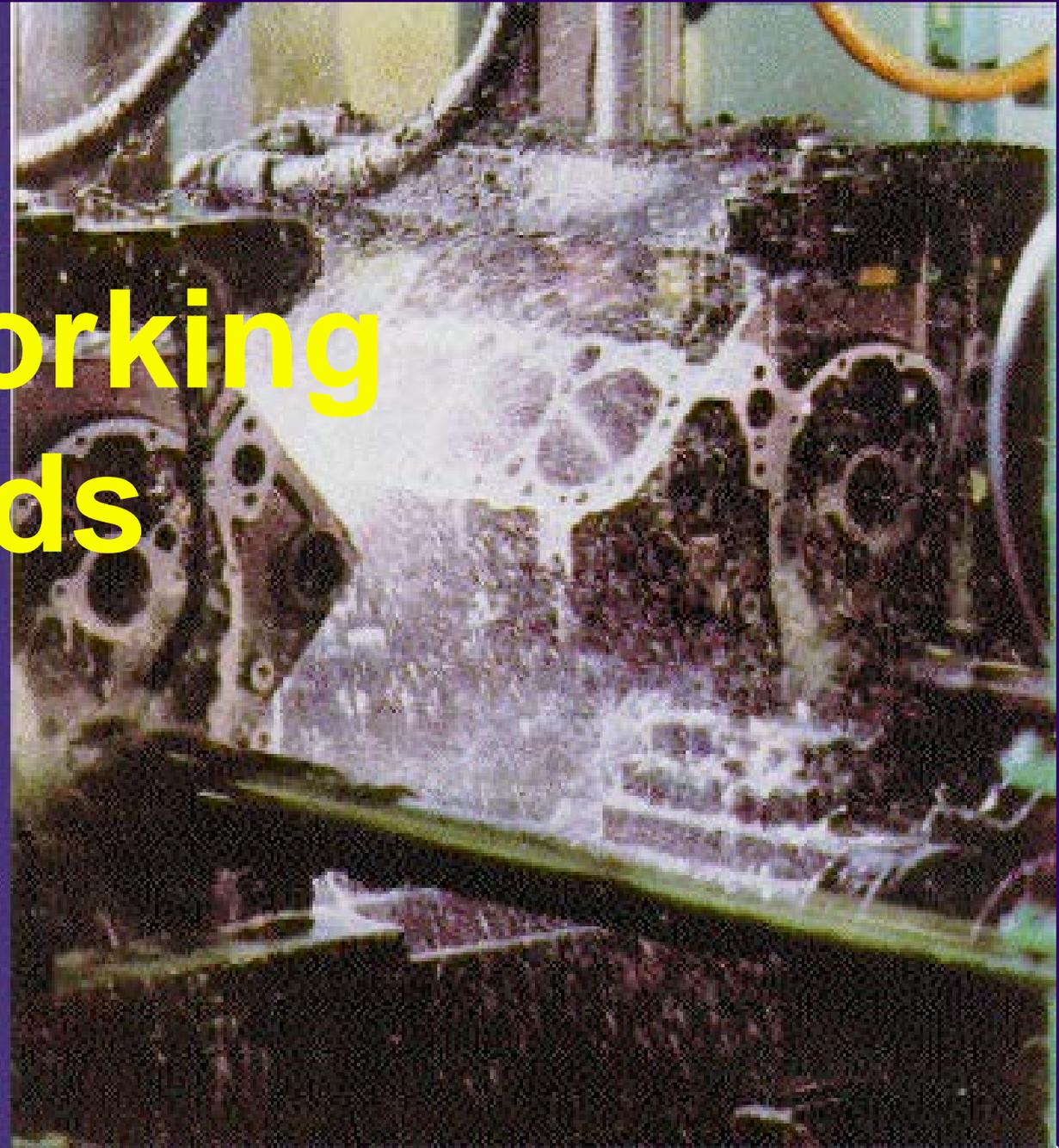


Comments on Technical Report Trim VX

Franklin E. Mirer, PhD, CIH
CUNY School of Public Health
fmirer@hunter.cuny.edu
NTP Report Review Subcommittee
February 16, 2016



Metalworking Fluids



History of the Project

- **UAW petition to NTP for bioassay of respiratory effects and carcinogenicity of representative MWF's – Supported by NIOSH**
- **Comments will address entire project**
- **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**

Significance

- **Respiratory effects of in-use MWF's of all types are generally accepted**
- **Multiple cohort studies report excess cancer mortality at various sites, but not consistently at a common site.**
- **NIOSH (1998) reported substantial evidence for association with cancer at multiple sites**
- **Eisen (2001) reported association with increased lung cancer**

Monograph 101 General Remarks

Associations with an increased incidence of cancer at various tumour sites were noted in the majority of these studies (Mirer, 2003, 2010; Savitz, 2003). In this volume of IARC Monographs and the previous Monograph (IARC, 2000), the Working Groups concluded that evidence from this body of literature could not be used for a specific evaluation of the carcinogenicity of diethanolamine because of the potential presence of other agents such as N-nitrosodiethanolamine (IARC Group 2B), poorly refined mineral oils and chlorinated paraffins. The Working Group did not evaluate the carcinogenicity of metalworking fluids as an exposure circumstance. The Advisory Group meeting that discussed future priorities for the IARC Monographs Programme (IARC, 2008) recommended that the evaluation of metalworking fluids should have medium priority

Composition of Test Materials

- For public health purposes, NTP must publish complete analyses of all 9 test articles
- Especially important for the 4 articles subjected to 90 day testing
- Classification as semi-synthetic or soluble oil is the marketing decision of manufacturer
- Master Chemical has already discontinued Trim VX

Trim VX MSDS

3. Composition/information on ingredients

Mixtures

Chemical name	Common name and synonyms	CAS number	%
SEVERELY HYDROTREATED PETROLEUM OIL		64742-52-5	30 - < 40
TRADE SECRET*		Proprietary*	10 - < 20
TRIETHANOLAMINE		102-71-6	3 - < 5

Material name: TRIM® VX

1278 Version #: 01 Issue date: 06-10-2015

SDS US
1 / 6

Chemical name	Common name and synonyms	CAS number	%
TRADE SECRET*		Proprietary*	1 - < 3
TRADE SECRET*		Proprietary*	1 - < 3
Other components below reportable levels			40 - < 50

*Designates that a specific chemical identity and/or percentage of composition has been withheld as a trade secret.



NTP Analysis - VX

TABLE 1

Measured Components of the Two Lots of TRIM VX Used in the Inhalation Studies of TRIM VX^a

Component	Lot 101607N^b	Lot 011509N^c
Water	7.1	6.8
Triethanolamine	3.7	3.2
4-Chloro-3-methyl-phenol	3.59	2.49
Diethylene glycol	0.87	1.07
Diethylene glycol monobutyl ether	1.02	1.11
Methyl palmitate	1.18	1.20
Methyl oleate	5.65	5.81
Methyl stearate	0.89	0.93
Myristic acid	0.49	0.23
Oleic acid	3.18	1.23
Palmitic acid	1.01	0.31
Propylene glycol	0.20	0.20
α -Terpineol	0.60	0.50
Hexane extractable material	80.2	85.0

^a All values are percentages
^b Used in the 3-month studies
^c Used in the 2-year studies

Sulfonate?

Water lost in sampling, doesn't count for exposure

Composition should be cleared up

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

MSDS extract Cimstar 3800

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

MSDS Trim SC210

2. COMPOSITION/INFORMATION ON INGREDIENTS

COMPONENT	OSHA PEL	ACGIH TLV	OTHER LIMITS RECOM.	CAS #	%RANGE
triethanolamine	none	5mg/m ³	none	102-71-6	10-20
petroleum oil	5mg/m ³	5mg/m ³	none	8002-05-9	1-10
monoethanolamine	3ppm	3ppm	none	141-43-5	1-10

The exact chemical identities and percentages of the raw materials used in TRIM® SC210 are trade secrets. This information is being withheld as provided for in the Occupational Safety and Health Administration's Hazard Communication Rule (29 CFR 1910.1200).

MSDS Syntilo 1023

Section 3. Composition/information on ingredients

Corrosion inhibitors and additives in aqueous solution.

Substance/mixture

Mixture

Ingredient name	CAS number	%
Triethanolamine	102-71-6	15-20
Di-isopropanolamine	110-97-4	5-10
borates, tetra, sodium salts-anhydrous	1330-43-4	1-5
Glycerin	56-81-5	1-5

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

Lung Tumors in male rats should be “some” evidence, not “equivocal”

- **Significance in poly-3 test is evidence for increased incidence and exposure response ($p = 0.007$)**
- **High dose exceeds historical controls**
- **Supported by similar monotonic increase in female rats (adenoma)**

Male Rats

Alveolar/bronchiolar Carcinoma ^e				
Overall rate ^f	0/50 (0%)	0/50 (0%)	0/50 (0%)	2/50 (4%)
Adjusted rate ^g	0.0%	0.0%	0.0%	4.8%
Terminal rate ^h	0/36 (0%)	0/39 (0%)	0/33 (0%)	2/34 (6%)
First incidence (days)	— ^j	—	—	729 (T)
Poly-3 test ⁱ	P=0.036	— ^k	—	P=0.221
Alveolar/bronchiolar Adenoma or Carcinoma ^d				
Overall rate	0/50 (0%)	0/50 (0%)	0/50 (0%)	3/50 (6%)
Adjusted rate	0.0%	0.0%	0.0%	7.2%
Terminal rate	0/36 (0%)	0/39 (0%)	0/33 (0%)	3/34 (9%)
First incidence (days)	—	—	—	729 (T)
Poly-3 test	P=0.007	—	—	P=0.106

Female Rats

Alveolar/bronchiolar Adenoma (includes multiple) ^l				
Overall rate	0/50 (0%)	0/50 (0%)	1/50 (2%)	3/50 (6%)
Adjusted rate	0.0%	0.0%	2.3%	6.8%
Terminal rate	0/30 (0%)	0/33 (0%)	1/33 (3%)	3/30 (10%)
First incidence (days)	—	—	731 (T)	731 (T)
Poly-3 test	P=0.024	—	P=0.511	P=0.127

Male + Female, Alveolar/bronchiolar Adenoma or Carcinoma

Overall	0/100	0/100	1/100	6/100
---------	-------	-------	-------	-------

“Clear” evidence for lung tumors in mice of both genders is the appropriate call.