SIXTH EDITION

PATTY'S TOXICOLOGY

VOLUME 6

EDITED BY

EULA BINGHAM

BARBARA COHRSSEN

WILEY

PATTY'S TOXICOLOGY

Sixth Edition

Volume 6

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Cumulative Chemical Index, Volumes 1–6
Cumulative CAS Index, Volumes 1–6

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Preface

In this Preface to the Sixth Edition, we acknowledge and note that it has been built on the work of previous editors. We especially need to note that Frank Patty's words in the Preface of the second edition are cogent:

> This book was planned as a ready, practical reference for persons interested in or responsible for safeguarding the health of others working with the chemical elements and compounds used in industry today. Although guidelines for selecting those chemical compounds of sufficient industrial importance for inclusion are not clearly drawn, those chemicals found in carload price lists seem to warrant first consideration.
>
> When available information is bountiful, an attempt has been made to limit the material presented to that of a practical nature, useful in recognizing, evaluating, controlling possible harmful exposures. Where the information is scanty, every fragment of significance, whether negative or positive, is offered the reader. The manufacturing chemist, who assumes responsibility for the safe use of his product in industry and who employs a competent staff to this end, as well as the large industry having competent industrial hygiene and medical staffs, are in strategic positions to recognize early and possibly harmful exposures in time to avoid any harmful effects by appropriate and timely action. Plant studies of individuals and their exposures regardless of whether or not the conditions caused recognized ill effects offer valuable experience. Information gleaned in this manner, though it may be fragmentary, is highly important when interpreted in terms of the practical health problem.

While we have not insisted that chemical selection be based on carload quantities, we have been most concerned about agents (chemical and physical) in the workplace that are toxicological concerns for workers. We have attempted to follow the guide as expressed by Frank Patty in 1962 regarding practical information.

This edition includes toxicological information on flavorings, metal working fluids, pharmaceuticals, and nanoparticles which were not previously covered, and reflects our concern with their technology and potential for adverse health effects in workers. It also continues to include the toxicology of physical and biological agents which were in the Fifth Edition. In the workplace of this new century, physical agents and human factors continue to be of concern as well as, nanotechnology. Traditionally, the agents or factors such as ergonomics, biorhythms, vibration, heat and cold stress were centered on how one measures them. Today, understanding the toxicology of these agents (factors) is of great importance because it can assist in the anticipation, recognition, evaluation and control of them. The mechanisms of actions and the assessment of the adverse health effects are as much a part of toxicology as dusts and heavy metals. As noted in Chapter 74 in Volume 5, the trend in toxicology is increasingly focused on molecular biology, mechanisms of action, and, molecular genetics.

The thinking and planning of this edition was a team effort by Barbara and Eula based on the framework that was established for the Fifth Edition by us and Charles H. Powell who died in September 1998. The three of us have had a long professional association with the Kettering Laboratory: Charles H. Powell received his ScD., Barbara Cohrssen received a MS, and Eula Bingham, has been a lifetime faculty member. Many of the authors were introduced to us through this relationship and association.

We are grateful for the help of our expert contributors, many of whom we have known for 10, 20 or 30 years, to complete this edition. The team effort was fostered between the current editors by many of the first contributors to Patty's such as Robert A. Kehoe, Francis F. Heyroth, William B. Deichmann, and Joseph Treon, all of whom were at the University of Cincinnati, Kettering Laboratory, sometime during their professional lives.

The authors have performed a difficult task in a short period of time for a publication that is as comprehensive as this one is. We want to thank Meghan Lobaugh whose assistance is greatly appreciated. We would like to express our deep appreciation and thanks to everyone who has helped us with this publication.

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San Francisco, California

USEFUL EQUIVALENTS AND CONVERSION FACTORS

1 kilometer = 0.6214 mile
1 meter = 3.281 feet
1 centimeter = 0.3937 inch
1 micrometer = 1/25,4000 inch = 40 microinches
= 10,000 Angstrom units
1 foot = 30.48 centimeters
1 inch = 25.40 millimeters
1 square kilometer = 0.3861 square mile (U.S.)
1 square foot = 0.0929 square meter
1 square inch = 6.452 square centimeters
1 square mile (U.S.) = 2,589,998 square meters
= 640 acres
1 acre = 43,560 square feet = 4047 square meters
1 cubic meter = 35.315 cubic feet
1 cubic centimeter = 0.0610 cubic inch
1 cubic foot = 28.32 liters = 0.0283 cubic meter
= 7.481 gallons (U.S.)
1 cubic inch = 16.39 cubic centimeters
1 U.S. gallon = 3,7853 liters = 231 cubic inches
= 0.13368 cubic foot
1 liter = 0.9081 quart (dry), 1.057 quarts
(U.S., liquid)
1 cubic foot of water = 62.43 pounds (4°C)
1 U.S. gallon of water = 8.345 pounds (4°C)
1 kilogram = 2.205 pounds
1 gram = 15.43 grains
1 pound = 453.59 grams
1 ounce (avoir.) = 28.35 grams
1 gram mole of a perfect gas ≈ 24.45 liters
(at 25°C and 760 mm Hg barometric pressure)
1 atmosphere = 14.7 pounds per square inch
1 foot of water pressure = 0.4335 pound per
square inch
1 inch of mercury pressure = 0.4912 pound per
square inch
1 dyne per square centimeter = 0.0021 pound per
square foot
1 gram-calorie = 0.00397 Btu
1 Btu = 778 foot-pounds
1 Btu per minute = 12.96 foot-pounds per second
1 hp = 0.707 Btu per second = 550 foot-pounds
per second
1 centimeter per second = 1.97 feet per minute
= 0.0224 mile per hour
1 footcandle = 1 lumen incident per square foot
= 10.764 lumens incident per square meter
1 grain per cubic foot = 2.29 grams per cubic meter
1 milligram per cubic meter = 0.000437 grain per
cubic foot

To convert degrees Celsius to degrees Fahrenheit: °C (9/5) + 32 = °F
To convert degrees Fahrenheit to degrees Celsius: (5/9) (°F − 32) = °C
For solutes in water: 1 mg/liter ≈ 1 ppm (by weight)
Atmospheric contamination: 1 mg/liter ≈ 1 oz/1000 cu ft (approx)
For gases or vapors in air at 25°C and 760 mm Hg pressure:
To convert mg/liter to ppm (by volume): mg/liter (24,450/mol. wt.) = ppm
To convert ppm to mg/liter: ppm (mol. wt./24,450) = mg/liter

CONVERSION TABLE FOR GASES AND VAPORS[a]

(Milligrams per liter to parts per million, and vice versa; 25°C and 760 mm Hg barometric pressure)

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
1	24,450	0.0000409	39	627	0.001595	77	318	0.00315
2	12,230	0.0000818	40	611	0.001636	78	313	0.00319
3	8,150	0.0001227	41	596	0.001677	79	309	0.00323
4	6,113	0.0001636	42	582	0.001718	80	306	0.00327
5	4,890	0.0002045	43	569	0.001759	81	302	0.00331
6	4,075	0.0002454	44	556	0.001800	82	298	0.00335
7	3,493	0.0002863	45	543	0.001840	83	295	0.00339
8	3,056	0.000327	46	532	0.001881	84	291	0.00344
9	2,717	0.000368	47	520	0.001922	85	288	0.00348
10	2,445	0.000409	48	509	0.001963	86	284	0.00352
11	2,223	0.000450	49	499	0.002004	87	281	0.00356
12	2,038	0.000491	50	489	0.002045	88	278	0.00360
13	1,881	0.000532	51	479	0.002086	89	275	0.00364
14	1,746	0.000573	52	470	0.002127	90	272	0.00368
15	1,630	0.000614	53	461	0.002168	91	269	0.00372
16	1,528	0.000654	54	453	0.002209	92	266	0.00376
17	1,438	0.000695	55	445	0.002250	93	263	0.00380
18	1,358	0.000736	56	437	0.002290	94	260	0.00384
19	1,287	0.000777	57	429	0.002331	95	257	0.00389
20	1,223	0.000818	58	422	0.002372	96	255	0.00393
21	1,164	0.000859	59	414	0.002413	97	252	0.00397
22	1,111	0.000900	60	408	0.002554	98	249.5	0.00401
23	1,063	0.000941	61	401	0.002495	99	247.0	0.00405
24	1,019	0.000982	62	394	0.00254	100	244.5	0.00409
25	978	0.001022	63	388	0.00258	101	242.1	0.00413
26	940	0.001063	64	382	0.00262	102	239.7	0.00417
27	906	0.001104	65	376	0.00266	103	237.4	0.00421
28	873	0.001145	66	370	0.00270	104	235.1	0.00425
29	843	0.001186	67	365	0.00274	105	232.9	0.00429
30	815	0.001227	68	360	0.00278	106	230.7	0.00434
31	789	0.001268	69	354	0.00282	107	228.5	0.00438
32	764	0.001309	70	349	0.00286	108	226.4	0.00442
33	741	0.001350	71	344	0.00290	109	224.3	0.00446
34	719	0.001391	72	340	0.00294	110	222.3	0.00450
35	699	0.001432	73	335	0.00299	111	220.3	0.00454
36	679	0.001472	74	330	0.00303	112	218.3	0.00458
37	661	0.001513	75	326	0.00307	113	216.4	0.00462
38	643	0.001554	76	322	0.00311	114	214.5	0.00466

CONVERSION TABLE FOR GASES AND VAPORS *(Continued)*

(Milligrams per liter to parts per million, and vice versa; 25°C and 760 mm Hg barometric pressure)

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
115	212.6	0.00470	153	159.8	0.00626	191	128.0	0.00781
116	210.8	0.00474	154	158.8	0.00630	192	127.3	0.00785
117	209.0	0.00479	155	157.7	0.00634	193	126.7	0.00789
118	207.2	0.00483	156	156.7	0.00638	194	126.0	0.00793
119	205.5	0.00487	157	155.7	0.00642	195	125.4	0.00798
120	203.8	0.00491	158	154.7	0.00646	196	124.7	0.00802
121	202.1	0.00495	159	153.7	0.00650	197	124.1	0.00806
122	200.4	0.00499	160	152.8	0.00654	198	123.5	0.00810
123	198.8	0.00503	161	151.9	0.00658	199	122.9	0.00814
124	197.2	0.00507	162	150.9	0.00663	120	122.3	0.00818
125	195.6	0.00511	163	150.0	0.00667	201	121.6	0.00822
126	194.0	0.00515	164	149.1	0.00671	202	121.0	0.00826
127	192.5	0.00519	165	148.2	0.00675	203	120.4	0.00830
128	191.0	0.00524	166	147.3	0.00679	204	119.9	0.00834
129	189.5	0.00528	167	146.4	0.00683	205	119.3	0.00838
130	188.1	0.00532	168	145.5	0.00687	206	118.7	0.00843
131	186.6	0.00536	169	144.7	0.00691	207	118.1	0.00847
132	185.2	0.00540	170	143.8	0.00695	208	117.5	0.00851
133	183.8	0.00544	171	143.0	0.00699	209	117.0	0.00855
134	182.5	0.00548	172	142.2	0.00703	210	116.4	0.00859
135	181.1	0.00552	173	141.3	0.00708	211	115.9	0.00863
136	179.8	0.00556	174	140.5	0.00712	212	115.3	0.00867
137	178.5	0.00560	175	139.7	0.00716	213	114.8	0.00871
138	177.2	0.00564	176	138.9	0.00720	214	114.3	0.00875
139	175.9	0.00569	177	138.1	0.00724	215	113.7	0.00879
140	174.6	0.00573	178	137.4	0.00728	216	113.2	0.00883
141	173.4	0.00577	179	136.6	0.00732	217	112.7	0.00888
142	172.2	0.00581	180	135.8	0.00736	218	112.2	0.00892
143	171.0	0.00585	181	135.1	0.00740	219	111.6	0.00896
144	169.8	0.00589	182	134.3	0.00744	220	111.1	0.00900
145	168.6	0.00593	183	133.6	0.00748	221	110.6	0.00904
146	167.5	0.00597	184	132.9	0.00753	222	110.1	0.00908
147	166.3	0.00601	185	132.2	0.00757	223	109.6	0.00912
148	165.2	0.00605	186	131.5	0.00761	224	109.2	0.00916
149	164.1	0.00609	187	130.7	0.00765	225	108.7	0.00920
150	163.0	0.00613	188	130.1	0.00769	226	108.2	0.00924
151	161.9	0.00618	189	129.4	0.00773	227	107.7	0.00928
152	160.9	0.00622	190	128.7	0.00777	228	107.2	0.00933

CONVERSION TABLE FOR GASES AND VAPORS (*Continued*)

(*Milligrams per liter to parts per million, and vice versa; 25°C and 760 mm Hg barometric pressure*)

Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter	Molecular Weight	1 mg/liter ppm	1 ppm mg/liter
229	106.8	0.00937	253	96.6	0.01035	227	88.3	0.01133
230	106.3	0.00941	254	96.3	0.01039	278	87.9	0.01137
231	105.8	0.00945	255	95.9	0.01043	279	87.6	0.01141
232	105.4	0.00949	256	95.5	0.01047	280	87.3	0.01145
233	104.9	0.00953	257	95.1	0.01051	281	87.0	0.01149
234	104.5	0.00957	258	94.8	0.01055	282	86.7	0.01153
235	104.0	0.00961	259	94.4	0.01059	283	86.4	0.01157
236	103.6	0.00965	260	94.0	0.01063	284	86.1	0.01162
237	103.2	0.00969	261	93.7	0.01067	285	85.8	0.01166
238	102.7	0.00973	262	93.3	0.01072	286	85.5	0.01170
239	102.3	0.00978	263	93.0	0.01076	287	85.2	0.01174
240	101.9	0.00982	264	92.6	0.01080	288	84.9	0.01178
241	101.5	0.00986	265	92.3	0.01084	289	84.6	0.01182
242	101.0	0.00990	266	91.9	0.01088	290	84.3	0.01186
243	100.6	0.00994	267	91.6	0.01092	291	84.0	0.01190
244	100.2	0.00998	268	91.2	0.01096	292	83.7	0.01194
245	99.8	0.01002	269	90.9	0.01100	293	83.4	0.01198
246	99.4	0.01006	270	90.6	0.01104	294	83.2	0.01202
247	99.0	0.01010	271	90.2	0.01108	295	82.9	0.01207
248	98.6	0.01014	272	89.9	0.01112	296	82.6	0.01211
249	98.2	0.01018	273	89.6	0.01117	297	82.3	0.01215
250	97.8	0.01022	274	89.2	0.01121	298	82.0	0.01219
251	97.4	0.01027	275	88.9	0.01125	299	81.8	0.01223
252	97.0	0.01031	276	88.6	0.01129	300	81.5	0.01227

[a] A. C. Fieldner, S. H. Katz, and S. P. Kinney, "Gas Masks for Gases Met in Fighting Fires," *U.S. Bureau of Mines, Technical Paper No. 248*, 1921.

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Contents

Metalworking Fluids (MWF)

Franklin E. Mirer, Ph.D., CIH

1 INTRODUCTION

There are two general categories and four major types of metal working fluid (MWF). The general categories are straight (generally mineral oils) and water reduced. The four major types of fluids are straight oils, soluble oils, semisynthetic fluids, and synthetic fluids. The water-reduced fluids include soluble and semisynthetic (straight oils diluted with water and additives) and synthetic (water and additives with no oil) (see Figure 96.1).

The additives include detergents, antioxidants, buffering agents, and antimicrobials. The water-reduced fluids come to the manufacturing facility as concentrates that are mixed into circulating systems, which may be single machine or large reservoirs. These mixtures may be further modified in use for process reasons.

The fluids include inevitable contamination by microbial products for the water-reduced metalworking fluids. Alternative names for MWF include metal removal fluid coolants, cutting oils, and machining fluid. MWF's may also be classified by purpose. Metal removal fluids is the term also used for fluids used in the cutting, grinding, drilling, broaching, and other operations for the manufacture of engines, transmissions, chassis parts, and other products. For these applications, the fluid is employed to lubricate, cool, and carry away swarf (chips) created by the manufacturing process. The characteristics and composition of fluids, as well as technological details of application have been reviewed by Byers and coauthors (1). The health hazards of MWF's and protective measures have been reviewed by NIOSH (2) and the OSHA Metalworking Fluids Standards Advisory Committee (3). Other reviews focusing on carcinogenicity have been conducted as well (4–8).

For the purposes of health risk assessment, the main categories are the distinction between straight oils and the water-based fluids. All the water-based fluids share the properties of the additive package, biocides and microbial products. This appears to be the most important distinction. Soluble and semisynthetic fluids also contain oils, essentially the same composition and with the same health effects as the straight oils.

The large majority of literature reviewed on human health effects below concerns mixed exposures to predominantly water-based fluids, with some straight oil operations in these facilities. Most of the experimental evidence is also from water-based fluids.

Subjects of human health effects studies were virtually all exposed to aerosols of fluids "in-use," that is, fluids with variable dilution, additional additives, microbial growth, tramp oil, and other debris as fluids exist in production equipment. The laboratory studies were largely performed on "virgin" undiluted or diluted concentrates, with a few including "in-use" fluids from production facilities.

Several agents known to be present in MWF's have been classified as carcinogenic and may be reviewed in other entries. These include mineral oils (9) of which are poorly refined mineral oils, are known to be carcinogenic to humans, and possibly carcinogenic such as *N*-nitrosodiethanolamine (6), chlorinated paraffins (10), diethanolomine (11), and coconut oil diethanolamide (11). In addition, formaldehyde may be present in the MWF environment as a product of formaldehyde release (triazine) biocides (12). Formaldehyde is known to be carcinogenic to humans (13).

Patty's Toxicology, Sixth Edition. Volume 6, Edited by Eula Bingham and Barbara Cohrssen.

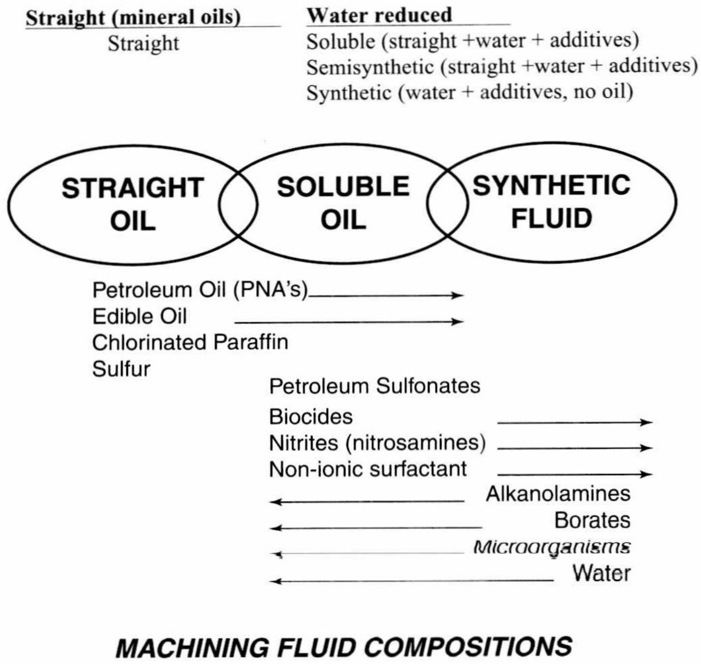

Figure 96.1. Metal working fluids.

2 METALWORKING FLUIDS: WATER-CONTAINING FLUIDS (SOLUBLE, SEMISYNTHETIC, AND SYNTHETIC FLUIDS)

2.1 Production and Use

NIOSH notes that more than 100 million gallons of metalworking fluids are produced every year, and more than 1 million employees are exposed to these MWFs (http://www.cdc.gov/niosh/blog/nsb100608_mwf.html).

2.2 Exposure Assessment

2.2.1 Air

MWF aerosols consist of a broad range of particle sizes. Very large particles are generated by mechanical action and from circulation of fluids. The airborne particles shrink as water and other volatiles evaporate; particles farther from point of generation are smaller. The "inhalable" fraction includes very large particles excluded by the closed face filter used by NIOSH 0500 for "total particulate." "Total" particulate includes particles larger than those in the "thoracic" fraction. Smaller particles are more easily captured by machine tool ventilation exhaust, but may pass through an air cleaner. Particles may be generated by evaporation and condensation from air cleaner filter media. Larger aerosol particles are more likely to be controlled by enclosures. Controlling metal removal fluid emissions on one machine will not affect background aerosol or other aerosol generated by other work stations; all machine tools need to be considered together. Air sampling using filter methods captures no water. Oil evaporates when captured on a filter, while nonoil additives to water soluble fluids do so to a much lesser degree (14).

2.2.2 Workplace Methods

Methods for measuring workplace exposure to MWF's are evolving. The most common method is NIOSH 0500 for gravimetric measurement of total particulate on a filter. The total particulate sampling device excludes the larger particles of the inhalable fraction. For this, an open-faced device or IOM sampler is needed. By contrast, thoracic fraction sampling will exclude a small fraction of those particles sampled by the total particulate filter. The American Society for Testing Materials (ASTM), a consensus organization, has proposed a number of methods for aerosol and bulk materials. ASTM D 7049, Test Method for Metal Removal Fluid Aerosol in Workplace provides a method for extracting the MWF fraction from total particulate. Additional test methods promulgated by the ASTM include E 1370 Guide for Air Sampling Strategies for Worker and Workplace Protection, E 1972 Practice for Minimizing Effects of Aerosols in the Wet Metal Removal Environment, E 2144 Practice for Personal Sampling and Analysis of Endotoxin in Metalworking Fluid Aerosols in Workplace Atmospheres, E 2169 Practice for Selecting Antimicrobial Pesticides for Use in Water-Miscible Metalworking Fluids, E 2563 Method for Enumeration for Non-Tuberculosis Mycobacteria in Aqueous Metalworking Fluids by Plate Count Method, E 2564 Method for Enumeration for Non-Tuberculosis *Mycobacteria* in Metalworking Fluids by Direct Microscopic Counting DMC) Method, E 2657 Method for Determination of Endotoxin Concentration in Water Miscible Metalworking Fluids.

2.3 Toxic Effects

The large majority of literature reviewed on human health effects below concerns mixed exposures to predominantly water-based fluids, with some straight oil operations in these facilities. Most of the experimental evidence is also from water-based fluids.

2.3.1 Experimental Studies

Concern for human health effects, notably respiratory effects, has driven most of the laboratory studies.

2.3.1.1 Acute Toxicity

2.3.1.1.1 Respiratory. Short onset inflammatory responses to short time exposure to virgin and in-use fluids have been studied in mice, rats, guinea pigs, and rabbits.

Schaper and coworkers evaluated the sensory and pulmonary irritating properties of aerosolized machining fluids in mice in a series of studies. In single exposure studies, water-reduced and straight oil fluids all induced sensory and pulmonary irritation. The synthetic/semisynthetic and soluble fluids were more potent irritants than the straight oils. Fluids collected from workplace operations (i.e., "in use" fluids) were found to be similar in potency to the same fluids prior to their introduction into the workplace (i.e., "neat" fluids) (15). The most potent fluids had three major components: tall oil fatty acids (TOFAs), sodium sulfonate (SA), and paraffinic oil (PO). Sensory irritation was due largely to TOFA, whereas SA produced pulmonary irritation (16). A fatty acid alkanolamide condensates and the triazine-type biocide largely contributed to the irritancy (17). A semisynthetic MWF and its components (alkanolamides, potassium soap, sodium sulfonate, and triazine) produced both sensory and pulmonary irritation (18).

Gordon and Harkema exposed rats to aerosols of used machining or unused machining fluid for 3 h/day for 3 days. A significant increase in total cells and neutrophils was observed not only in animals exposed to the used MWF but also in the nasal septum of animals exposed to unused machining fluids (no measurable endotoxin). The investigators concluded that in addition to endotoxin, nonendotoxin components of machining fluids may contribute to the increase in sputum and chronic bronchitis reported for workers exposed to machining fluid aerosols (19).

Also in the rat, exposure to MWF-containing endotoxin resulted in a time- and concentration-dependent migration of neutrophils in the lung tissue's interstitial spaces as well as the lavageable airways. A population of alveolar macrophages was observed to be enlarged in size and demonstrated increased sensitivity to oxidative metabolism. The investigators suggested that while endotoxin contamination of MWF is capable of producing an acute inflammatory event, other predisposition factors may be required to induce alterations in pulmonary physiology (20).

Gordon exposed guinea pigs to nebulized water, unused machining fluid, or used machining fluid. At the end of a 3 h exposure, specific airway conductance decreased in a dose-dependent manner by exposure to aerosols of the used machining fluid. Acute lung injury was evidenced by changes in cellular and biochemical indices in lavage fluid. Animals exposed to aerosols of the endotoxin-free unused machining fluid had statistically significant adverse functional, cellular, or biochemical effects at highest but not lower exposures. These results suggest that contamination of machining fluid during use or storage may lead to the adverse respiratory effects of aerosolized machining fluids (21).

In the guinea pig, Thorne and DeKoster observed that in-use MWF was consistently more toxic than the corresponding virgin (neat) MWF. Removal of microorganisms by filtration of the in-use MWF did not change the responses observed in either strain. These studies demonstrate that lung inflammation may be an important outcome from exposure to in-use MWF and that endotoxin is a toxicant of importance (22).

Also in the guinea pig, Gordon examined the relative toxicity of three major classes of machining fluids (soluble, semisynthetic, and synthetic) as well as that of unused (fresh) versus used (grab samples taken from manufacturing sites) machining fluids. Relative toxicity in guinea pigs to respirable aerosols of unused machining fluids was semisynthetic > soluble >> synthetic. Greater toxicity was observed in animals exposed to used, machining fluid aerosols compared to unused fluids. Within the used machining fluid types, significantly greater adverse effects were observed in animals exposed to poorly maintained fluids (i.e., heavy microbial contamination) versus well-maintained fluids. Changes in biochemical and cellular parameters in bronchoalveolar lavage fluid occurred after a single exposure to poorly maintained used machining fluid aerosols. Changes in inflammation but not lactate dehydrogenase and protein were observed in animals repeatedly exposed to semisynthetic machining fluid aerosols. A statistically significant increase in lavage fluid neutrophils was observed in guinea pigs exposed to 5 mg/m^3 used, semisynthetic machining fluid aerosols for 4 weeks. In separate experiments, physicochemical properties of unused machining fluids were found to contribute to the production of adverse effects. Adjustment of the alkaline and hypotonic nature of the unused semisynthetic machining fluid to isotonicity and pH 7 significantly reduced adverse effects. Together, these findings strongly suggest that multiple factors contribute to the adverse respiratory effects associated with occupational exposure to machining fluid aerosols (23).

Airway hyper-responsiveness (AHR) to water-soluble cooling lubricants (CLs) induced by aerosol administered by tracheal tube was studied in a rabbit model of occupational lung disease. A commercial boric acid amine ester without biocide was compared to a sulfonate type with biocide. Inhalation of 2.0% ACH almost doubled the dynamic elastance in the ACH challenge test in this animal group. CL aerosols with and without biocide in the range of 50 and 5 mg/m^3 applied via tracheal tubes increased AR to ACH within 4 h of exposure in a time- and concentration-dependent manner. It has to be assumed that this augmented AR indicates an increased risk of developing lubricant-induced obstructive lung diseases (24).

Dalbey and coworkers reported subchronic studies with aerosolized mineral base oils and lubricants in unspecified species. Exposures to aerosols of mineral base oils resulted mainly in concentration-related accumulation in the lung of alveolar macrophages laden with oil droplets. Inflammatory cells were observed with higher aerosol concentrations, consistent with the clinical literature from highly exposed workers. Additives in some formulated products and/or maintenance of mineral-based metalworking fluids may play a much more significant role in potential health effects (25).