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Mixing Unknown Unknowns

Testing TSCA and GHS against Metalworking Fluids

BY FRANK MIRER

In my former position as director of health and safety for the United Auto Workers, I participated in many meetings about chemical exposures in which UAW members would “invent” for themselves the goals of the Toxic Substances Control Act. They would say that chemicals should be tested before the members themselves were exposed, the dangerous chemicals eliminated and the others controlled to “safe” levels. Of course, TSCA was in effect, and it wasn’t doing the job. UAW’s comments on TSCA in 1976 noted that the Act’s emphasis on “new” chemicals was incomplete. The UAW believed that the main danger to workers (and communities) came from existing chemicals and products that were mixtures, including metalworking fluids (MWFs).

Early UAW and other studies had found excess mortality from cancer among workers exposed to MWFs in the manufacture of engines, transmissions, and other parts for autos. These findings led to jointly administered research funds, which launched more extensive studies of MWFs. A Harvard team published results showing increased respiratory issues in 1989 and increased cancer in 1992. In 1993, the UAW petitioned OSHA for a standard for MWFs; NIOSH for a criteria document, which was issued in 1998; and EPA for a TSCA testing rule.

Section 4 of TSCA, “Testing of Chemical Substances and Mixtures,” provides EPA with the authority to compel manufacturers to conduct chronic exposure studies for respiratory and cancer effects. UAW’s intent was to identify the specific ingredients responsible and relative potencies of mixtures so that substitutes could be found or other control measures imposed.

I met with a staffer at EPA (name and date lost to memory) who said there was no need for testing, since OSHA would regulate exposure to the lowest feasible level if my claims on epidemiology were correct, and anyway it

would take years to promulgate a rule to require testing, which would not be a priority. I judged that the UAW could never litigate our way to a testing rule.

CARCINOGENIC POTENTIAL

Eventually, the UAW tried to litigate to an OSHA standard. There were many steps between UAW’s 1993 petition, OSHA’s final denial of the petition in 2003, and a 3rd Circuit Court of Appeals decision in 2004 flushing the case. The three judges noted:

There is little doubt, and it is not disputed here, that exposure to MWFs can have debilitating health effects.... While there is little debate about the link between MWF exposure and respiratory disorders and dermatitis (again, the debate is over the severity and prevalence), the evidence supporting a connection to cancer is equivocal at best.

The opinion gave OSHA a free ride to say no to any petition for a standard, based on OSHA’s unreviewable claim of priorities and resources. So both the Court and OSHA viewed carcinogenic potential as key. And a conclusion of carcinogenic potential depended in part on laboratory evidence.

With EPA’s testing rule off the table,

the National Toxicology Program’s recently published toxicity studies on MWFs offer another road to data. This extensive toxicology program identified “representative” MWFs and resulted in two reports on chronic studies and two on ninety-day studies. The key findings were:

- A two-year chronic study of a soluble oil formulation found “clear” evidence for carcinogenicity in lungs for both genders of rats and “equivocal” evidence for both genders of mice.
- A study of a semi-synthetic MWF found “some” evidence for carcinogenicity in female mice (lung and thyroid) and equivocal evidence in both genders of rats.
- As reported in a paper published online this past July by *Toxicology and Industrial Health*, the ninety-day studies for four representative MWFs found essentially 100 percent respiratory histopathology of at least one diagnosis at the lowest dose tested—10 mg/m³ for the chronic and 25 mg/m³ for subchronic.
- Of the additional five MWFs considered, short-term studies (genetic toxicology) were not predictive of chronic results for all nine, including the two found carcinogenic in two-year studies.

The Independent Lubricant Manufacturers Association and other groups commented extensively to discourage this NTP “testing” program, to minimize the health findings during the peer review, and to claim that effects could not be generalized to formulations not tested.

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THE KNOWN UNKNOWNNS

Based on the results of NTP's vigorous "testing" effort, some conclusions can be drawn:

1. Respiratory histopathological effects of considerable gravity were shown for uncontaminated water-based MWFs. These results counter the (incorrect) claim by critics of the NTP studies that respiratory problems were entirely caused by poor treatment of MWFs, so no enforceable OEL was needed, only MWF maintenance.
2. The most authoritative review of MWF epidemiology, by an IARC working group, considered a large number of studies and concluded that a majority demonstrated associations between MWFs and "increased incidence of cancer at various tumor sites." Previously critics, although not conceding this conclusion, could argue that effects of past exposure seen in current studies were due to known carcinogens in past MWFs, such as nitrosamines, less refined oils, diethanolamine and certain chlorinated paraffins, all of which were removed by formulators in response to laboratory studies. The NTP findings provide biological plausibility to the epidemiology and support a concern for continuing risk from current MWFs.
3. How the effects observed in these studies can be generalized to the hundreds of MWFs now in use is a matter of debate. In my opinion it would be reckless to claim that warnings on Safety Data Sheets for the MWFs studied by NTP don't also apply to different soluble, semi-synthetic, or synthetic MWFs. In contrast, were these studies to be "null" for health effects, I would expect some management groups to argue the findings were totally generalizable. In the alternative, each MWF formulation should be subjected to testing.
4. The results of the ninety-day studies can be used to set a reference concentration or OEL for respiratory histopathology. Uncertainty factors should include extrapolations for LOAEL to NOAEL or benchmark dose, animal to human, and human variability. My judgment is that the resulting OEL would be materially less than the 0.4 mg/m³ REL promulgated by NIOSH in 1998.
5. There's not a straight line between findings of respiratory pathology and warnings on an SDS. I fear that the "weight of the evidence" based on "professional judgment" by manufacturers (who are also marketers) permitted by OSHA's GHS-infused Hazcom Standard will be a defense to citations issued for no warnings.
6. My view, based on nearly 25 years of contesting the issue of MWFs, is that these results

would have shifted the balance toward a standard if we had them in 2000 or before. Remember, TSCA has been around since 1976.

7. The carcinogenic potential of carcinogens is invisible to a ninety-day study. Carcinogenic potential, or its absence, can be evaluated only by two-year studies in which the maximum tolerated dose (MTD) is achieved, and results are analyzed with mortality-adjusted statistics and against an extensive collection of control results in the strains of animals employed. (There's a separate argument that lifetime studies rather than those terminated at two years are more sensitive and should be employed.)
8. Short-term studies, including two-week whole-animal studies, provide little evidence for absence of toxic potential after chronic exposure. The two-week study mainly provides information for setting the MTDs for ninety-day tests.

More generally, the dangers of chemical exposures can be divided into "known knowns," "known unknowns," and "unknown unknowns." For exposures with recognized toxic potential and potency—these are the known knowns, which clearly need enforceable exposure limits and other protections—setting OSHA standards or TSCA Section 6 rules is the priority, although TSCA testing rules might fill in some gaps

in knowledge. My judgment is there are dozens of these exposure situations, not hundreds.

Unknown unknowns are partly addressed by TSCA reporting requirements, which might be mined more rigorously. TSCA reform may shift the balance of power and make more information available for such chemicals.

The known unknowns, which will be studied according to their prioritization within EPA's existing chemicals program, are where the action is, and where effort should be applied. That's a matter of political will at EPA and the effectiveness of advocates for worker health, in both labor and management, to generate that political will. ☹

RESOURCES

- International Agency for Research on Cancer: IARC Monographs Volume 101, <http://bit.ly/iarc101> (PDF, 2013).
- NTP: Technical Report on the Toxicology and Carcinogenesis Studies of TRIM VX in Wistar Han [Cr:Wi (Han)] Rats and B6C3F1/N Mice, <http://bit.ly/ntp591> (PDF, February 2016).
- NTP: Technical Report on the Toxicology Studies of Cimstar 3800 in F344/Ntac Rats and B6c3f1/N Mice and Toxicology and Carcinogenesis Studies of Cimstar 3800 in Wistar Han [Cr:Wi (Han)] Rats and B6c3f1/N Mice, <http://bit.ly/ntp586> (PDF, September 2015).
- *Toxicology and Industrial Health*: "Comparative Pulmonary Toxicity of Inhaled Metalworking Fluids in Rats and Mice" (July 2016).