

Needs for Public Health Intervention and Needs for New Research on Vinyl Halides and Their Polymers: A Public Policy Perspective

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Consideration of needs for public health interventions and new research requires comparative assessments of the health benefits that are likely to result from alternative uses of limited regulatory and technical resources. This paper briefly examines regulatory and research priorities in the light of recent information on the carcinogenic hazards of vinyl chloride and alkyl and vinyl halides related to vinyl chloride, the respiratory-system hazards of poly (vinyl chloride), and the reproductive hazards of vinyl chloride. Specific suggestions are made for relatively promising types of efforts in these areas.

Introduction

The papers presented in this conference represent a considerable expansion of available information on the hazards of vinyl chloride, poly(vinyl chloride), and vinyl bromide. There are also useful reviews of previously available literature on a broad range of other alkyl and vinyl halides. In this session, the focus shifts from the often slow and deliberate process of expanding what we "know" about carefully circumscribed questions in VC/PVC toxicology/epidemiology to what at first glance will seem a much more speculative process. Judgments must be made about appropriate priorities for regulation ("public health intervention") and for new research—and for purposes of making such judgements it is important not only to understand what we can be said to know today about a restricted set of well-researched hazards, but what is ultimately likely to be true and worth knowing about the whole range of alternative hazards which could be the targets of research and regulatory efforts.

For purposes of setting regulatory policies, we

need to ask, "Where is there likely to be a relatively large amount of harm occurring which is likely to be relatively easily preventable by using the intervention tools at hand?" Some of the modes of intervention available either to OSHA or EPA for addressing different kinds of problems include: conventional OSHA time-weighted-average exposure limits for specific air contaminants, enforced by industrial hygiene inspections (best adapted to hazardous exposures which are concentrated in a few establishments with relatively large numbers of workers exposed per establishment, for most productive use of limited industrial hygiene inspection manpower); limitations on the manufacture or sale in interstate commerce of specific chemicals or formulations for specific high-hazard uses, under the Toxic Substances Control Act (best adapted to hazardous exposures which occur in dispersed locations in industry as a result of the use of specific industrial chemical products, e.g., degreasing and dry-cleaning solvents); efforts to redirect dosage away from unusually sensitive subgroups of workers or prevent effects by preventive medical surveillance, mandated in OSHA standards; and "generic policy" standards (e.g., the recent generic OSHA carcinogen policy) designed to facilitate standard-setting and stimulate "voluntary" corporate action in ad-

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vance of standard-setting for a range of hazards deemed to pose similar types of issues for public policy.

For purposes of assessing priorities for research relevant to public health, we need to ask, "Where is there an opportunity to significantly reduce uncertainties in the benefits of candidate public health intervention measures, using the research tools at hand?" The relevant research tools here include not only toxicological and epidemiological research into likely health effects, but also technological research on control methods and innovative development of safer industrial processes.

The present paper will attempt to address these questions of regulatory and research needs in the light of recent information on three topic areas that are the subjects of this conference: the carcinogenic hazard of vinyl chloride, and alkyl and vinyl halides related to vinyl chloride, the respiratory-system hazards of poly(vinyl) chloride and the reproductive hazards of vinyl chloride. Through the details of these separate subjects, there is one theme that will emerge—both scientists in considering research opportunities and policy makers in considering public health interventions need to structure their efforts to have the widest possible application. Policy makers must seek sensitive points of leverage in the world, where a limited intervention may be expected to produce substantial health benefits for a large number of people. Scientists must seek the critical experiments which contribute to the establishment of generalized rules or principles, with application to the widest possible set of questions of public health significance.

Carcinogenic Hazards of Vinyl Chloride and Related Compounds

Does the information that has become available over the last few years suggest that a new round of public health initiatives to further reduce the eventual incidence of vinyl chloride cancers is likely to achieve greater health protection benefits than alternative uses of the same technical, standard-setting and enforcement resources? In order to give an affirmative answer to this question, it would be necessary (though not necessarily sufficient) for us to draw two conclusions from available information about vinyl chloride: (a) that there is a substantial chance that long-term exposure to vinyl chloride at the current standard level of 1 ppm poses an appreciable risk, and (b) that a new round of OSHA standard setting and enforcement would

lead to substantial reductions in current average worker exposures to vinyl chloride.

With respect to the first question, I think there is substantial basis for concern that the current 1 ppm vinyl chloride standard may pose an appreciable carcinogenic risk to workers. As part of a 1976 retrospective assessment of the benefits and costs of the original OSHA 1 ppm standard (1), my colleagues and I made projections of likely human risk based on the available data from Dr. Maltoni's BT1 (rat) and BT4 (mouse) results (2), an assumption of linear dose-response kinetics at low doses, and four alternative sets of rules for translating the rodent vinyl chloride dosages to equivalents for human workers. (Basically, the four alternative rodent/human extrapolation rules arose from the four permutations of the choice between expressing dosage as milligrams/body weight vs. milligrams/body surface area and the choice of whether or not to divide the rodent dosage by 35 to adjust for the 35-fold difference between rodent and human lifespans.) These projections suggested that a year of worker exposure to vinyl chloride at the current OSHA 8-hr limit of 1 ppm might be expected to lead to an additional cancer risk from all tumors of between 1×10^{-4} and 3×10^{-2} for the four different extrapolation rules. Even the lower of these figures implies that some tenths of a percent of workers exposed over an appreciable portion of a working lifetime at the standard level may expect to develop an occupationally related cancer; if one of the more pessimistic (higher) extrapolation rules should prove more nearly correct, the ultimate toll might well be in the tens of percent for long-exposed workers.

On examination of the more complete animal carcinogenesis data presented by Dr. Maltoni, it appears that projections of roughly the same order of magnitude would be made based on the more recently available information. The one possible exception is the appreciable excess of mammary cancer which appears to persist at relatively low exposure levels.

Data from studies in humans modify this picture slightly. The preliminary epidemiological information which is available to date does not seem to be indicating as large a risk among workers exposed to vinyl chloride in the past as might be expected under the more pessimistic extrapolation rules from the animal data. For example, the best guess one might make from the data of Dr. Weber for German chemical industry workers with and without exposure to past high levels of vinyl chloride is that the vinyl chloride workers appear to show an excess of deaths from all malignancies amounting to something like 6% of the total deaths which have occurred so far in that cohort. It should be stressed,

of course, that because of the decades-long latency period for most occupational cancers, it is likely that the final percentage of past vinyl chloride-exposed workers who develop occupational cancers will be higher than that observable among the deaths which have occurred to date.

In sum, prudent people in both government and industry must consider that a real chance remains that chronic worker exposure at the level of the current 1-ppm standard may carry an appreciable cancer risk. As new production and control technology become available over the coming years there should be a regular, continuing program to implement superior processes and reduce worker exposure as far below 1 ppm as is technically feasible. Available data suggest that the Swedish PV polymerization industry is now operating with average worker exposures in the range of 0.2 to 0.3 ppm (3). My impression from talking with OSHA industrial hygienists and from the observation that as of 1976-77 over 90% of vinyl chloride samples from OSHA inspections were in compliance with the 1 ppm standard (4), is that this kind of performance may also be being achieved in the U.S.

I think it is doubtful, however, that a new round of formal OSHA standard-setting on vinyl chloride would represent the most productive use of the agency's limited resources at this time. Even within the family of alkyl and vinyl halides which have been discussed at this conference, there are materials which, even if they prove to be some orders of magnitude less potent as carcinogens than vinyl chloride, are likely to yield greater public health benefits from intervention. The PVC polymerization industry has several thousand workers, exposed to vinyl chloride on average in the range of tenths of a ppm. Because of the major pressures placed on the vinyl chloride/poly(vinyl chloride) production industries over the past several years, it seems unlikely that there are still many available but unexploited techniques for making further order-of-magnitude reductions in exposure. On the other hand, the number of workers in the dry cleaning industry is in the hundreds of thousands (5), and available data indicate exposures to perchloroethylene in the high tens and low hundreds of ppm (6). Metal degreasing operations may offer another similar picture with respect to exposure to trichloroethylene. Solvent and chemical intermediate uses of ethylene dichloride and pesticidal and fuel additive uses of ethylene dibromide may also place substantial numbers of people at risk in situations where many of the relatively easy technical measures to reduce exposures have not yet been implemented. Even though the available data

on the carcinogenicity of some of these materials is not as conclusive as for vinyl chloride, and relative potencies are highly uncertain, the dangers of widespread cancer and related risks and likely untapped opportunities to control exposures suggest that they should be placed relatively higher on OSHA and EPA priority lists for public health interventions than vinyl chloride.

After this extended discussion of intervention priorities it will perhaps not be surprising that I see the importance of further scientific work on vinyl chloride primarily in terms of its potential to produce generalizable lessons for quantitative animal-to-human extrapolations, to advance understanding of the dynamics of metabolism of precursor substances to active carcinogenic intermediates, and to provide a set of reasonable technical expectations relevant to future risk assessments for chemicals related to vinyl chloride.

The epidemiological observations on worker groups with previous exposure to vinyl chloride clearly need to be pursued in future years. However, in the future, much more disaggregated data should be made widely available for analysis using different approaches for separately assessing the effects of duration of exposure, calendar year of exposure, age at which exposure occurred, relative level of exposure and years of follow-up relative to the years of exposure. Because of the observed "saturation" of some vinyl chloride tumor responses observed in animals (2), it is important not simply to assume in analyzing the epidemiological data that high-level short-term exposures will have the same effects as low-level long-term exposures that deliver the same total dose.

Epidemiological observations on the large worker groups exposed to dry cleaning solvents have already yielded tentative indications of excess cancer incidence in some cases (7). Further ongoing epidemiological work on these populations is clearly of major importance. In preparation for possible positive findings in these efforts, I think it would be prudent now to foster creative technological development work to understand the options for alternative dry cleaning/degreasing solvent systems and equipment to make large reductions in worker exposures, should that be eventually called for.

Finally, further observations in animal systems should seek biochemical explanations for the ways in which the quantitative vinyl chloride carcinogenic response changes with dosage, animal strain and bodily tissue. Given such knowledge, comparative studies with other alkyl and vinyl halides may provide better quantitative guidance on likely carcinogenic dose response curves for this whole family of related chemical agents.

Respiratory-System Hazards of Poly(vinyl Chloride)

The elegant study presented by Dr. Seaton, supported by the studies and case reports of other workers, indicates quite clearly that long-term exposures to fine PVC dust (less than 5-10 μm in size) can lead to chronic declines in standard measures of lung function. In considering public health interventions based on these results, I would suggest again that two questions be asked: (a) do the present data give us reason to suspect that fine PVC dust is much more hazardous per unit of exposure than other miscellaneous organic and inorganic dusts with comparable particle size ranges that are not regulated under OSHA's "nuisance dust" exposure standard, and (b) how extensive is the PVC dust problem likely to be relative to the problem posed by other particulates.

Taking the latter question first, it appears from the presentation of Dr. Wheeler on poly(vinyl chloride) processes and products that PVC preparations with predominantly small particle sizes are mainly produced by a relatively small sector of the industry that uses the "emulsion" polymerization process. Given this, and the possibility that even for this sector of the industry in the future, much of the material could be marketed in wet form now that the dust hazard is becoming recognized, it seems likely that a coercive intervention aimed specifically at fine PVC resin producers and consumers might yield relatively small benefits.

On the other hand, the problem of exposure to miscellaneous "nuisance" dusts in general is clearly common in many different industries. I think it is likely that a general reappraisal of policies and standards with regard to miscellaneous particulates in respirable size ranges might well lead to significant long term benefits in the prevention of chronic pulmonary impairment. To build an appropriate database for such a reappraisal, I would suggest that in conjunction with the next round of NIOSH's National Occupational Hazard Survey, there should be a cross-sectional survey of lung function among workers exposed for many years to various kinds of respirable particulates (controlling, of course, for past smoking habits and other relevant factors). Based on the results of such a survey and other relevant data, policy-makers could determine what regulatory distinctions should be made between different kinds of fine particulate matter. At the very least, it seems likely that the term "nuisance" as applied to miscellaneous dusts should be done away with if, as I suspect, there is a general observation that long term exposures to fine par-

ticulates is associated with an increased risk of impaired lung function.

Before leaving this subject I would like to make one additional plea to researchers doing epidemiological work on potential chronic respiratory hazards. For purposes of policy analyses on possible standards, it is vital that data be presented not only in terms of average losses in lung function among populations as related to exposure and age characteristics, but also in terms which allow the full reconstruction of the population distribution of lung function values as related to exposure and age. Potentially important changes at the tails of population distributions of lung function may be obscured unless the basic regression analyses which determine average effects are supplemented by presentations which reveal what is happening to subgroups which for other reasons have better or worse lung function than average.

Reproductive Hazards of Vinyl Chloride

For this area too, it seems to me that an effort to resolve the general issues posed by reproductive hazards in the workplace and set a "generic policy" standard will be likely to have greater long term public health benefits than an attempt to promulgate a standard which is narrowly focussed on the reproductive hazards of vinyl chloride. There are some very important general issues which need resolution, and the educational effects of the policy-making process alone could have substantial widespread beneficial effects through changes in current practices in industry.

Beyond the reduction of exposures—which should be pursued to the maximum extent feasible—designing appropriate medical surveillance and compensated removal programs for workers exposed to reproductive hazards is a very delicate and controversial subject. Many women, in particular, are justifiably fearful that newly won employment opportunities may be eroded and that attempts to eliminate women with child-bearing potential from employment in specific jobs have the effect of reinforcing the old notion that women's primary function in society is to make babies. Cases of real abuse in company medical removal policies have been alleged in the lead industry in which some women have apparently felt forced to choose between their jobs and undergoing sterilization operations.

Adding to the concern of women over unequal treatment has been the fact that male mutagenic

risks have not received the same level of attention with respect to medical removal as have female teratogenic risks. Exposure of reproductively active males to mutagens is thought to generally pose greater mutagenic risks than exposure of females, because male reproductive cells divide continuously throughout life, whereas female reproductive cells do not usually divide after birth until fertilization. In epidemiological studies of mutation rates for point mutations, mutagenic risks generally show a stronger positive correlation with paternal age than with maternal age (8).

I believe that with care and sensitivity to these issues, it is possible to design medical removal protection programs which reduce teratogenic and mutagenic risks while not infringing on individual rights or other social values. A reasonable general approach could include a full and frank disclosure to all exposed workers of the known and suspected mutagenic and teratogenic risks of the substances with which they are working. Removal, with economic protection, at the worker's option, should be triggered by the intention of the worker to have children, sufficiently in advance of conception to allow the substance(s) of concern to be eliminated from the body before the critical events which occur in each sex. For prevention of mutagenesis in males, reduction of the body burden of the substance of concern to the desired protective level should occur some months before conception, to allow sensitive postspermatogonial stages in the development of sperm to be purged from the system. Return to the previous job can be safely permitted after conception is confirmed, provided that precautions are taken against transport of the hazardous substance home on the worker's clothing. For prevention of teratogenesis in pregnant women, reduction of the substance of concern to the desired protective level should occur prior to conception. Return to the previous job should probably

wait either until the completion of the pregnancy or the completion of lactation, depending on an assessment as to whether the substance poses hazards to the child by way of the mother's milk.

In conclusion, I would like to reiterate, that in considering priorities both for public health interventions and for research, it is often helpful to step back a few paces from the immediate problems at hand. With careful consideration of the generic issues posed by specific problems related to vinyl chloride, I think both scientists and policy makers alike can direct their efforts toward projects with greater payoff than would be realized by straight forward extensions of previous efforts.

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