RISK MANAGEMENT OF EXISTING CHEMICALS

Proceedings of a Seminar
Conducted

December 8-9, 1983
Washington, D.C.

Sponsored by:

Chemical Manufacturers Association

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CHAPTER 10

VINYL CHLORIDE AND TSCA

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INTRODUCTION

The well-known regulatory history of vinyl chloride and its role as a bellwether of current regulatory philosophy makes it a useful paradigm for examining the relationship of existing laws and the Toxic Substances Control Act (TSCA) for control of chronic hazards.

To this end, we will first review some of the highlights of its regulatory history, and then engage in some speculation as to the response these events might elicit today under TSCA.

INDUSTRIAL AND COMMERCIAL USE OF VINYL CHLORIDE

Vinyl chloride became of industrial importance about fifty years ago, approximately a hundred years after its discovery, when Semons discovered that its polymer could be converted into useful articles by plastization with phthalate esters. Commercial development began first in Europe and then in this country in the late

1/ Air Products and Chemicals, Inc., 1983.

thirties, largely using existing rubber processing equipment, for it was rubber which it initially replaced in the market. For the same reason, the use of polyvinyl chloride (PVC) was sequestered by the government during the war years, and it was not until the early fifties that widespread consumer applications developed. PVC is now a mature product, and its growth rate falls in step with the Gross National Product. Presently, about six billion pounds are used annually in this country, and about four times that in the world.

Some of the broader toxicological attributes of vinyl chloride (VC) were recognized in the thirties. It was known to be an anesthetic, but problems with cardiac arrythmia prevented its use in that application.[2/] As pathological techniques improved, industry scientists recommended in the early sixties that exposure be limited to 50 ppm, because of temporary liver enlargement in animals at that level,[3/] but the American Conference of Governmental and Industrial Hygienists considered this overly conservative and accepted instead the 500 ppm recommendation of Harvard scientists.[4/] This was the value adopted by the Occupational Safety and Health Administration (OSHA) in its formative days.

Also in the early sixties, the European industry recognized among its workers a disease termed acroosteolysis, AOL, which is a degenerative disease of the bone tufts, particularly in the fingers, that is accompanied by Reynaud's phenomenon.[5/] An extensive epi-

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2/ W. F. von Oettigin, "The Halogenated Hydrocarbons, Their Toxicity and Potential Dangers," Public Health Service Publication No. 414 (Washington, D.C.: U.S. Department of Health, Education and Welfare, 1955).

3/ T. R. Torkelson, F. Oyers, and V. K. Rowe, "The Toxicity of VC as Determined by Repeated Exposures of Laboratory Animals," American Industrial Hygiene Association Journal, XXII (1961), p, 354.

4/ American Conference of Governmental and Industrial Hygienists, "Documentation of the Threshold Limit Value, 1963" (Cincinnati, OH, 1963).

5/ S. Suciu, J. Drejman, and M. Valaskai, "Study of Diseases Caused by Vinyl Chloride," Medical Intern., XV (1963), p. 967.

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demiological survey here and in Europe found about a hundred possible cases which were associated closely with manual cleaning of reactor walls between polymerization batches, but neither the precise etiological agent nor the disease mechanism was identified.[6/]

An attempt was made to reproduce this disease in rats by the medical department of one of the European producers. An exact duplication of the human disease was not seen, but many of the rats developed tumors at numerous sites. The reporting of this finding by Viola[7/] in 1970 evoked little interest in the regulatory community, possibly because of the very high doses used, several thousand ppm, which were frankly toxic to the animals, and the fact that the tumors were largely metastatic from the Zymbal gland, an organ not present in humans.

Nevertheless, both the European and domestic producers formed consortia to perform bioassays at lower concentrations and also began epidemiological surveys of their employees.

Preliminary results of the European bioassay became available first in early 1973, and showed tumor development at much lower concentrations in organs which do have human counterparts. This result was transmitted to regulatory officials that summer, and industry screening of employee records was intensified.[8/] This resulted in the recognition that winter by an industry medical director of a cluster of three rare liver tumors termed angiosarcoma, ASL, in the employees of one facility.[9/] The reporting of this fact to

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6/ W. A. Cook, et al., "Industrial Hygiene Evaluation of Thermal Degradation Products from PVC Fetus in Meat-wrapping Operations," Arch. Environ. Health, XXII (1971), p. 74. Also, B. D. Diman, et al., "Occupational Acroosteolysis I, An Epidemiological Study," Ibid., p. 61.

7/ P. L. Viola, "Pathology of Vinyl Chloride," Medicina del Lavoro, LXI (1970), p. 174.

8/ A. W. Barnes, "ICI Ends Its Silence on Vinyl Chloride," Chemical Engineering News, (July 8, 1974), p. 21.

9/ J. L. Creech and M. N. Johnson, "Angiosarcoma in Workers Exposed to Vinyl Chloride as Predicted for Studies in Rats," Journal of Occupational Medicine, XVI (1974), p. 150.

government officials led to the current regulatory status of vinyl chloride.

It also led to a virtual explosion of research on the chronic toxicity of VC. The body of scientific literature on the oncogenicity of vinyl chloride is as large as that for any other substance. It is recognized that VC is a classical procarcinogen. Metabolism by the mixed function oxidase in the liver converts it to the ultimate carcinogen, an epoxide. Detoxification of this intermediate by the sulfhydryl group of glutathione or other proteins removes the toxic potential.[10/] Both of those mechanisms are saturable.[11/] An overload of the metabolic step assures that the vinyl chloride will pass through the liver and some will be metabolized in other organs. An overload of the detoxification step allows escape of the toxicant into the sinusoidal passages of the liver where interaction with the chromosomal protein causes ASL to develop. An overload of both mechanisms can lead to tumor development outside of the liver, as is seen in mice and rats at very high doses. Despite the large data base, however, information on the precise mechanism of these various steps still is lacking. We do not even understand why some persons respond with AOL and some with ASL, but none with both diseases.

REGULATORY STANDARDS

OSHA proceeded promptly in early 1974 to set an emergency temporary limit of 50 ppm for worker exposure, and later that year reduced the limit to one ppm, the current figure. Industry was given a grace period during which respirators could be used to meet this requirement, but now that level must be met by engineering practices.[12/]

10/ W. K. Lelbach and H. J. Marsteller, "Advance in Internal Medicine and Pediatrics" Springer-Verlag, XLVII (New York, 1981).

11/ R. Hefner, P. Watanabe, and P. Gehring, "Percutaneous Absorption of Vinyl Chloride Gas in Rhesus Monkey," Toxicology and Applied Pharmacology, XXXIV (1975), p. 529.

12/ OSHA Standard for Vinyl Chloride, 29 CFR 1910.1017.

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The Environmental Protection Agency (EPA) promulgated a combined engineering and works practice standard in 1976 which has resulted in ambient concentrations in the fractional ppb range near producing or using facilities.[13/]

In the meanwhile, the Food and Drug Administration (FDA) and Consumer Product Safety Commission (CPSC) established prohibitions on the use of VC in aerosol or other consumer applications, a practice which had been discontinued in 1973. The Bureau of Alcohol, Tobacco and Firearms of the Treasury Department (BATF) had already banned the use of PVC liquor bottles in 1973 because of concern for taste effects from migration of residual VC into the contents. In 1975 the FDA proposed revocation of the generally regarded as safe (GRAS) status of rigid PVC packaging under the Delaney clause, also because of migration concerns, but that proposal never has been promulgated, and the FDA has stated that it is considering withdrawal of the proposal and recommending to BATF the reauthorization of plastic liquor bottles in light of the current very low residual monomer levels in fabricated PVC articles.

Other regulations have followed as new statutes and rules have come into play. The Department of Transportation (DOT) and the Coast Guard regulate the transportation of VC, of course, and VC is listed as a priority pollutant and hazardous waste under various water and solid waste rules, and has a reportable quantity of one pound under Superfund.

Did the existing laws operate satisfactorily at the time of discovery of the chronic hazards of VC? It appears that they did. A leading medical authority who was deeply involved in the worker health evaluation in 1974 has termed VC a "success story." Reevaluation of the risk to employees under the one ppm standard by a conservative nonthreshold extrapolation method[14/] yields a lifetime estimate of less than 10^{-8}, a risk level which is not thought to be of concern. The comparable risk estimate for the general populace is

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13/ EPA Standard for Vinyl Chloride, 40 CFR 61.60.

14/ P. J. Gehring, P. G. Watanabe, and C. N. Park, "Risk of Angiosarcoma in Workers Exposed to Vinyl Chloride as Predicted for Studies in Rats," Toxicology and Applied Pharmacology," XLIX (1979), p. 15.

several orders of magnitude lower. EPA has stated on several occasions that it believes that vinyl chloride is regulated adequately.

RISK ASSESSMENT

Risk assessment has been a popular avocation among those interested in VC, and more than a dozen have been performed.[15/] These can be divided generally into two classes: those which rely solely on animal data; and those which attempt to incorporate the human experience.

Those in the first class yield similar results, and show the normal spread of estimates from the various mathematical models in common use. These range from 1,500 to 10^{-5} ppb for a lifetime risk of 10^{-6}, or eight orders of magnitude. It is necessary to eliminate the high-dose data points, that is, those over 2,500 ppm from the Maltoni data[16/] in order to get reasonable fits to most models, because these doses show broad systemic toxicity. The lower doses, 500 ppm and below, as a group fall into a general pattern on a log-probit plot, but individual two or three dose experiments show tremendous differences in slope when plotted separately. The popular multihit model predicts a lifetime risk of 10^{-6} at fractional ppb levels.

The human factor was accounted for in two ways. The EPA used some preliminary employee epidemiological data to confirm its animal-based extrapolation.[17/] Unfortunately, the human data were

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15/ J. T. Barr, "Risk Assessment for Vinyl Chloride in Perspective," (Paper 82-9.2 presented at the 75th Annual Meeting of the Air Pollution Control Association, New Orleans, LA, 1982), Lines 20-25.

16/ C. Maltoni, et al., "Vinyl Chloride Carcinogenicity Bioassays (BT Project)," (Paper presented at "Le Club de Cancerogenese Chemique," Institute Curie, Paris, November 10, 1979).

17/ A. M. Kusmack and R. E. McGoughy, "Quantitative Risk Assessment for Community Exposure to Vinyl Chloride," (Washington, D.C.: U.S. Environmental Protection Agency, December 5, 1975).

selected from those locations known to have ASL cases, while other facility data were omitted. They also were in error on the past exposures by more than an order of magnitude. This resulted in an estimate of 20 cases per year from the estimated 1974 ambient concentrations for the population within five miles of production and processing facilities.

The EPA seldom bothers to check its estimates against available data, so it sometimes comes up with results such as that made for arsenic a few years ago that would have predicted 18 million cases of skin cancer a year in this country if it had been applied to Agency data on the average arsenic concentrations in drinking water. Similarly, a survey of all known ASL cases in this country for the ten years before 1974 showed no cases associated with residency near such plants,[18/] rather than the 200 predicted cases. It is reasonable to assume that if any cases had developed since that time, the publicity associated with it would have brought them to light. Thus we have 110 million-person years of negative history for nearby residents. This places an upper limit on risk of less than 10^{-7} per ppm-yr.

Two studies applied pharmacokinetics in an attempt to obtain relevant human data. Gehring and coworkers estimated a lifetime risk of 10^{-8} at one ppm from the probit model, based on a biotransformation of rat data. The unconstrained linear model predicted no risk at less than 99 ppm.[19/]

Anderson, Hoel and Kaplan carried this procedure one step further, and applied it to bound metabolic products, rather than to the total amount metabolized. Their results gave a lifetime risk of 10^{-7} at less than one ppm, with the probit model, or at less than two ppm with the linearized multistep model.[20/]

18/ H. Popper, et al., "Development of Hepatic Angiosarcoma in Man Induced by Vinyl Chloride, Thorotrast, and Arsenic," American Journal of Pathology, XCII (1978), p. 349.

19/ P. J. Gehring, P. G. Watanabe, and C. N. Park, Toxicology and Applied Pharmacology, XLIX (1979), p. 15.

20/ M. W. Anderson, D. G. Hoel, and N. L. Kaplan, "A General Scheme for the Incorporation of Pharmacokinetics in Low-dose Risk Estimation for Chemical Carcinogens. ibid., LV (1980), p. 154.

Thus we see that risk is in the eye of the estimator, but it is clear that estimates incorporating human data reflect the human experience for VC far better than do the direct application of animal data.

There was understandable uncertainty on the part of both the regulators and industry in 1974. This was the first commodity chemical to be regulated under the relatively new statutory situation as the result of new information. Nevertheless, both the regulatory agencies and industry acted promptly to reduce exposures and emissions to an acceptable level.

The current count of occupational ASL cases is about 100 worldwide, with 30 of these in this country.[21/] All these cases had their first exposure in 1964 or earlier, and there appears to be room for optimism that the steps taken in the mid-sixties because of the AOL information will have prevented any significant number of cases developing from exposures commencing after that date. Certainly it is reasonable to expect that there have been no new cases initiated after the early seventies.

Had TSCA been in place in the mid-sixties, would it have made any difference in the course of events? It appears unlikely that it would. Certainly the AOL discovery would have resulted in a series of 8(e) notices to TSCA. The probable outcome of that would have been either a recommendation from the Interagency Testing Committee (ITC) for more tests, or a Section 4 testing requirement. It is possible that, because of its commercial importance, VC could have been placed on the ITC list before the AOL data became available. Additional data could have been called for under Sections 8(a) and (d). The result of all this most likely would have been a negotiated testing rule, under which industry would have initiated a series of studies which would have culminated in a bioassay, and the carcinogenicity of VC would have been discovered in due time. Yet, this is precisely what did happen in the absence of TSCA, except that the preliminaries were omitted, and the bioassay was performed concurrently with the screening tests. Thus it is possible that the

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21/ J. Stafford, personal communication, Liver Angiosarcoma Cases, April 15, 1983.

final critical data were obtained earlier than would have occurred under present conditions.

Bear in mind that most of today's powerful testing methods were not available twenty years ago. That fact would not have been changed by legislative fiat, and any decision made at that time had to be made in light of the available knowledge.

If the data of Viola suddenly became available today instead, would there be any significant difference in the outcome, or the timing of that outcome? Probably so, but only because of the vastly more powerful scientific tools which we have available to us now. Neither the speed of agency motion nor the rate at which industrial facilities can be built or modified has increased. If anything, the latter has slowed, given the multiplicity of permits and approvals now required. Overall, it is possible that if today we knew nothing more about VC than was known in 1970, we would arrive at a regulated state a few months earlier than was achieved in 1974, but scientific progress, and not legislative or regulatory advancement, should get the credit.

What if VC were to become a new product today? Would it run the same course in which it would be 40 years before there was full recognition of its chronic potential? Certainly not. Again, however, the reason is due more to scientific progress rather than statutory development.

One change might be apparent. If VC were the subject of a Premanufacture Notification (PMN) today, rather than being the model to which all other aliphatic olefins are compared for structure-activity analysis, it would be judged by the others in its family. This comparison would be less dogmatic than the reverse is now. Ethylene and vinylidene chloride are not animal carcinogens; the relevance to humans of the carcinogenicity of high doses of trichloroethylene (TCE) is equivocal and controversial; and vinyl acetate has only a preliminary "non-negative" report. Thus, this class of substances would have lost its leader for structure activity comparison, and a decision as to the need for further testing from that analysis would not be clear-cut, based on analogous compounds.

Neither would a full minimum premanufacture data (MPD) set be of any great assistance. VC responds poorly to the classical in-vitro tests, and only recently has it become possible to obtain reproducible positive results in many of these. If the position were taken

that any positive result triggers further testing, then we would be left exactly where we were in the late sixties, recognizing the need for a bioassay.

One other point should be considered before the requirements of Section 9 of TSCA to give primacy to existing statutes is ignored. Section 2 of TSCA requires the consideration of economic factors in actions taken under TSCA, while the Occupational Safety and Health Act and the Clean Air Act Section 112 do not. In fact, at the time that VC was being regulated, these two statutes were being interpreted as forbidding economic consideration. Had TSCA been the regulatory vehicle of 1974, it is unlikely that the final regulations could have been as strict as they actually became, because of this factor.

It is difficult to separate cleanly the compliance costs for the OSHA and EPA rules on VC because of the overlapping time periods. The best estimate for OSHA costs made by the industry in a presentation to the Presidential Task Force on Regulatory Relief was something over $200 million of capital, with over $25 million per year of annual costs. The EPA has reported to Congress[22/] that compliance with its rule has cost about $100 million per year since 1978. Thus, about $900 million has been expended thus far. Various published costs per life saved have ranged from $4 to $200 million for the OSHA standard, depending on which exposure starting point was used. The more costly EPA standard appears not to have prevented any cases of ASL, based on epidemiology, and thus has an infinite cost.[23/] This suggests that the proponents of strong TSCA activity for existing chemicals should reconsider their position on Section 9 if their long-term goal is more stringent regulations.

There seems to be no sure method of preventing some surprises in toxicology. Improved surveillance and diagnostic methods assure that we will know more about chronic effects in the future than we do now. New substances simply cannot be subjected to full-scale

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22/ Environmental Protection Agency, "The Cost of Clean Air and Clean Water," (Annual Report to Congress, Senate Document 96-38, December, 1979).

23/ J. T. Barr, "Risk Assessment for Vinyl Chloride in Perspective."

testing before they show strong commercial promise. If there were no other reasons for this, the limitation on test facilities dictates that we direct our immediate effort toward substances of major import, and this is being done at capacity. It is proper that we concentrate our efforts on present exposures. Fortunately, recent medical advances help us to recognize these surprises earlier, and to minimize their impact.

Existing statutes, that is, non-TSCA derived regulations, appear to be able to regulate existing substances adequately. The history of vinyl chloride bears this out. The principal value of the TSCA derived activities seems to be in the gathering of surveillance data on these substances to assure that the relevant data are made available to the proper agencies, and in future oversight of new substances as they develop into commercial items.

SUMMARY AND CONCLUSIONS

The reexamination of the hazards of all existing chemicals is an overwhelming task for which EPA has no special expertise.[24/] Just the establishment of priorities for such a reexamination is beyond the present capacity of the Agency.[25/] The Agency has recognized some of the problems which it faces, and the recent "TSCA Priorities and Progress, 1983" report discusses a much more sharply delineated existing chemicals program. Even here, however, the division between TSCA and existing statutes is not defined clearly. Further, the Agency appears to be entering the realm of risk management through its Advisory and Chemical Hazard Information Profile (CHIPs) series. One unfortunate result of this is the generation of another tainted list of substances which becomes an invitation for pressure to regulate. The temptation to prepare these

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24/ National Research Council, "Regulating Pesticides," (Washington, D.C.: Environmental Studies Board, Committee on National Resources, 1980).

25/ J. T. Barr, "Establishing Regulatory Priorities," Toxic Substances Journal, IV (1983), p. 290.

"little lists" for the executioners apparently is too great to be resisted,[26/] as Lester Lave pointed out recently.

We believe that EPA can best obey its statutory mandate by developing a more efficient system for establishing priorities, and by implementing more effectively its Section 9 procedures.

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26/ Lester Lave, "The High Cost of Regulating Low Risks," Wall Street Journal, August 19, 1983.

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