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MANUFACTURING CHEMISTS ASSOCIATION

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R. N. WHEELER

November 19, 1971

To: Participants in the November 16, 1971 Vinyl Chloride Conference

Subject: Report on Proceedings of the Conference Held at the Hotel Washington, Washington, D. C.

Attendance:

Anthony, M. V.	Stauffer Chemical Company
Bell, Z. G.	PPG Industries, Inc.
Cassidy, L. E.	Canadian Industries, Ltd.
Duffield, D. P.	ICI Ltd.
Fedoruk, J. C.	Allied Chemical Company
Fritz, R. J.	Esso Chemical Company
Gabbett, J. F.	Pantasote Company of New York
Hendricks, N. V.	Standard Oil Company (N.J.)
Johnson, M. N.	Monsanto Company
Johnson, K. D.	Manufacturing Chemists Association
Knapp, W. A.	Allied Chemical Company
Knoepfel, R. W.	Solvay American
Lefevre, M. J.	Solvay et Cie
Lindquist, A. B.	Stauffer Chemical Company
McCormick, W. E.	The B. F. Goodrich Company
Madden, W. W.	Firestone Plastics
Mudd, J. R.	General Tire & Rubber Company
Pitts, S. P.	Continental Oil Company
Siegel, A. C.	Tenneco Chemicals, Inc.
Sheth, K. K.	Allied Chemical Company
Smith, W. M.	Air Products and Chemicals, Inc.
Torkelson, T. R.	The Dow Chemical Company
Weekers, Pierre	Solvay et Cie
Wheeler, R. N.	Union Carbide Corporation
White, N. G.	Shell Chemical Company
Zwicker, B.M.G.	The B. F. Goodrich Company

Our present awareness of the alleged carcinogenicity of vinyl chloride monomer has resulted from studies begun in an effort to elucidate the mechanisms of pathogenesis of the acroosteolysis seen in some vinyl chloride workers. As most of the companies represented at this meeting were participants in, or otherwise



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concerned with, the Case Registry project at the University of Michigan, Dr. K. D. Johnson (MCA staff representative) led off the meeting with a brief report of the status of the project. He requested an indication of the interest of the project sponsors in an extension of the program beyond the exhaustion of currently committed funds, and pointed out that there is now on deposit with MCA to the credit of the individual project sponsors, adequate funds for the maintenance of the Registry for several more years.

Upon a showing of interest by the delegates present, Dr. Johnson agreed to send copies to each sponsor of the University of Michigan proposal for a project extension, together with a report of his remaining credit and anticipated cost for the indicated contract extension. He extended to any companies, not now a project sponsor, that have employees at risk and that may wish to become a party to the study, an invitation to request more detailed information on programs and costs from him at MCA. (Note: subsequent to the Conference, MCA received a University of Michigan proposal estimating a cost of \$4,000 per year for the maintenance of the Registry and its records.)

Mr. N. V. Hendricks summarized the recent events and publications which had alerted the industry to the reported tumorigenic properties of vinyl chloride, and called upon Mr. McCormick to report on the studies of this problem that had been made by MCA's Occupational Health Committee.

Mr. McCormick reviewed the literature reports, and summarized the information that had been received from Dr. P. L. Viola, the principal investigator in the reported studies, during a visit to the U. S. by Dr. Viola under the sponsorship of a group of interested companies. On the basis of these data, a suggested research protocol has been developed, and cost estimates secured from a number of competent consulting laboratories for the performance of the specified tests.

Dr. Marcel Lefevre traced the experience of Solvay et Cie with industrial hygiene problems associated with vinyl chloride synthesis and polymerization, and defined the relationship of his company to Dr. Viola's studies, both past and current. He revealed that additional exposure studies, at seven concentration levels, are now underway with a "composite" source of vinyl chloride, 50% acetylene derived and 50% from ethylene dichloride.

It appeared that any U. S. research should seek answers to three questions:

- (1) Are the tumorigenic properties of the vinyl chloride used in his studies by Dr. Viola related to vinyl chloride, per se, or to impurities present?



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(2) If impurities are implicated, are the significant contaminants uniquely related to one or another of the commercial vinyl chloride synthesis methods?

(3) If the pertinent carcinogen can be identified, can a "no-effects" level be demonstrated?

Inasmuch as the material used by Dr. Viola was of undocumented composition, and variously noted to contain from 1 to 3 percent impurities, and whereas American commercial practice now may specify total organic impurities to as low as 100 ppm (99.99% assay), some hope, but not great confidence, was expressed that it could be shown that Dr. Viola's results were attributable to the impurities in his sample. Mr. Knoepfel volunteered to attempt to identify the production lots from which Dr. Viola had secured his samples, and to secure available analytical data on such lots. The qualitative list of the impurities reported by Dr. Viola as present in his material is appended to this report of proceedings.

Mr. McCormick reviewed the test protocol his group had suggested, and expressed his view that current plans should contemplate the eventual need of an epidemiological survey of workers with possible exposure to potentially carcinogenic concentrations of atmospheric contaminants in vinyl chloride operations. He commented thereby that the \$183,000 low bid must be considered as just the start of the anticipated project costs, and that any epidemiology or protocol expansion could substantially increase the funding requirements.

The suggestion that research costs be reduced by limiting the tests with acetylene-derived material to the highest exposure level only, primarily as a "positive control," received general support.

The problems of defining routes of funding or concurrence on a specific test protocol led to the decision to appoint a smaller study group to reach agreement on these points and to report the results of their deliberations in the form of a specific research proposal with specific funding requirements and mechanisms. One of the major questions posed to this group was the extent to which tests should be planned on a concurrent basis, to save time, or on a sequential basis, to minimize investment in tests subsequently shown to be unnecessary or non-informative.



The following individuals were designated to serve on this group. Subsequent consultation with MCA management determined that these individuals could most appropriately operate as a planning group, without specific ties to any standing MCA technical committee, with oversight on behalf of MCA through its staff representative, Dr. K. D. Johnson. When and if they present a research proposal to MCA with a request for MCA administration, the Board will at that time, as a part of any such project authorization, define lines of organizational supervision and reporting for the industry steering committee set up to guide the project.

Ad Hoc Planning Group for Vinyl Chloride Research

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The main conference adjourned at 2:45 P.M., and the Planning Group convened. They agreed that:

- (1) vinyl chloride manufacturers should be solicited for analytical data on their commercial grade of vinyl chloride, listing identified impurities and their characteristic ranges, methods of analysis, and limits of detection;
- (2) their interest be determined in contracting for the provision of a supply of vinyl chloride of uniform quality over the life of the research project, including their proposed specifications and analytical verification of specification conformance;
- (3) the Planning Group's proposal should include a recommendation for funding on a sharing of costs prorated among participating vinyl chloride producers and polymerizers on the basis of total capacity (monomer synthesis plus PVC production, each taken separately, as published in Oil, Paint and Drug Reporter and/or the Stanford Research Institute's Directory of Chemical Producers, is shown in attachment to this report);
- (4) that discussions with the offering laboratories be continued to clarify cost changes associated with suggested protocol modifications, and that Drs. Lane, M. N. Johnson, and Torkelson and Messrs. Hendricks and McCormick review test protocols in the light of new information developed at the conference, and prepare recommendations on a "best value" research protocol; and
- (5) the next meeting be held in Washington, Tuesday, December 14, at 9:00 A.M. (as the MCA Conference Room is not available at that time, MCA will arrange for a meeting room space in a convenient hotel, and will notify members of the Planning Group as soon as space can be confirmed.)

Respectfully submitted,


Kenneth D. Johnson
Staff Representative

KDJ/cj
Enclosures (3)



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Reported Production Capacity
Million P unds/Year

Company	Vinyl Chloride Monomer	Poly- vinyl Chloride	Total	Percent * of Total
Air Products & Chem.	---	170	170	1.9
Allied Chem. Corp.	300	140	440	4.9
American Chem. Corp.	170	70	240	2.7
Atlantic Tubing & Rubber	---	100	100	1.1
Borden, Inc.	---	240	240	2.7
Continental Oil Co.	600	155	755	8.4
Diamond Shamrock	---	250	250	2.8
Dow Chemical	1220	---	1220	13.6
Ethyl Corp.	420	125	545	6.1
Firestone T & R	---	240	240	2.7
General T & R	---	75	75	0.8
B. F. Goodrich	1000	600	1600	17.8
Goodyear T & R	---	90	90	1.0
Great American	---	70	70	0.8
Keysor Century	---	50	50	0.6
X Monochem <i>Monomer</i>	300	---	300	3.3
Monsanto	---	150	150	1.7
Occidental Petroleum	---	360	360	4.0
Olin Corp.	---	150	150	1.7
Pantasote Co.	---	110	110	1.2
PPG	800	---	800	8.9
Stauffer	---	150	150	1.7
Tenneco	255	190	445	4.9
Union Carbide	---	350	350	3.9
UNIROYAL	---	135	135	1.5
	5065	3970	9035	100

*This column represents the approximate share of project costs that would be borne by the indicated company if all named companies elected to participate. Since this is not likely, percentage costs prorated among participating companies may be expected to be somewhat larger than that shown.

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1000
1400
2000



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VINYL CHLORIDE



200 ppm (Approximately ~~200~~⁵⁰⁷ mg/m³)

Vinyl chloride is a flammable gas with anesthetic properties at high concentrations. At anesthetic concentrations (8 to 12%) it has serious effects on cardiac muscle resulting in arrhythmias and sensitization in dogs(1,2). There is a wide margin between anesthetic and lethal concentrations (30-40%)(3). Torkelson, Oyen and Rowe(4) reported that repeated seven-hour exposures for six months at 200 ppm resulted in histologic changes in the central lobular region of the livers of rabbits, but not in rats, guinea pigs and dogs. At 100 ppm there was only slight liver enlargement. A subsequent report by Lester, Greenberg and Adams(5) on the effects of repeated exposure of rats to vinyl chloride assaying 99 + percent purity at 2 and 5% concentration stated that, although liver changes were noted, they were not considered to be of pathological significance. In their opinion, a recommended TLV of 500 ppm was satisfactory for worker exposure.

An interim report was made by Mutchler and Kramer(6) of long industrial health experience with vinyl chloride workers. Beginning in 1950, continuous monitoring was begun at five or six stations and the results compared with breath analyses(7) for vinyl chloride for 50 workers. Between 1950 and 1967 the mean air concentration was 160 ppm, with one maximal peak at 600 ppm of vinyl chloride and with great daily variation from 30 to 170 ppm, on the average. During part of this time vinylidene chloride* was an associated air contaminant estimated at around 5 ppm. Twenty-one clinical parameters were measured for comparison with the environmental data, and relationships were obtained by stepwise multiple linear regression analysis. Of medical examinations numbering 404 on 97 workers, 66 were used for comparison with 650 controls. These examinations with final diagnoses made according to the international classification of diseases, failed to reveal any overt condition attributable to vinyl chloride (or vinylidene chloride) exposure. No differences of physiologic significance were found in blood pressure, hemoglobin, electrocardiograms, and no body abnormalities (acro-osteolysis) appeared. No one was clinically ill. Six clinical parameters appeared to be altered, however. Among these, beta lipoprotein, icterus index, and bromosulfalein retention time may have some physiologic significance. The investigators felt, from a review of the interim findings, that a time-weighted average exposure concentration at 300 ppm (combined vinyl chloride and 5 ppm vinylidene chloride) could result in some degree of liver dysfunction. The multiphasic screening tests are continuing on all exposed workers, and analysis of the findings is being made on an individual worker basis. In the meantime, a time-weighted average threshold limit value of 200 ppm vinyl chloride (with a few ppm vinylidene chloride) seems appropriate to prevent adverse systemic effects from long-continued daily exposure.

(* A 90-day animal inhalation exposure to vinylidene chloride at 5 ppm was without observable effect.)

References:

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3. Mastromatteo, E., Fisher, A.M., Christie, H., Danziger, H.: *Am. Ind. Hyg. Assn. J.* **21**, 394 (1960).
4. Torkelson, T.R., Oyen, F., Rowe, V.K.: *ibid.* **22**, 354 (1961).
5. Lester, D., Greenberg, L.A., Adams, W.R.: *ibid.*, **24**, 265 (1963).
6. Mutchler, J.E., Kramer, C.G.: Report on Relation of Exposure to State of Health of Dow Chemical Workers, Gordon Conf., Tilton, N.H. (August, 1968).
7. Baretta, E.D., Stewart, R.D., Mutchler, J.E.: *Am. Ind. Hyg. Assn. J.* **30**, 537 (1969).

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