

Manufacturing Chemists Association

Minutes of Meeting

0021

VINYL CHLORIDE RESEARCH COORDINATORS

MCA Conference Room

November 28, 1973

MEMBERS PRESENT:

T. R. Torkelson, Chairman
T. R. Aalto for
Marvin Rosen
Z. G. Bell, Jr.
W. D. Harris
Richard Henderson
for M. R. Gasque
C. A. Johnson

M. N. Johnson, M.D.
H. L. Kusnetz for
R. L. Maycock
A. B. Lindquist
W. E. Rinehart

The Dow Chemical Company
Tenneco Chemicals, Inc.

PPG Industries, Inc.
UNIROYAL, Inc.
Olin Corporation

The Goodyear Tire & Rubber
Company

The B. F. Goodrich Company
Shell Chemical Company

Stauffer Chemical Company
Ethyl Corporation

OBSERVERS PRESENT:

D. P. Duffield, M.D.
Perry Gehring

ICI Mond Division
The Dow Chemical Company

MCA STAFF PRESENT:

A. C. Clark
K. D. Johnson

1. Bis Chloromethyl Ether as a Possible Vinyl Chloride
Impurity

The question has been raised as to the possibility that Bis-CME might constitute one of the unidentified peaks sometimes found in vinyl chloride gas chromatograph tracings. Although there is no reason to suspect that such contamination might be responsible for the tumors found in VCM-exposed rats, since these tumors are not of the variety

CONFIDENTIAL

RSV 0000521

caused by Bis-CME exposures, the subject hypothesis does remain a theoretical possibility, and manufacturers with such unidentified but detectable impurities in their VCM may find it desirable to ascertain the identity or non-identity of such peaks with Bis-CME.

2. Report on "Meat Wrappers" Asthma Syndrome

Copies of the paper by Sokol, Aelony and Beall (JAMA 226, 639-641 - 1973) were distributed to those present. An earlier report by Bobby F. Kraft (now with NIOSH) on this topic was mentioned, and the Secretary was asked to procure and distribute copies. It was the consensus of the Research Coordinators that the syndrome here reported was not related to vinyl chloride monomer, but that, by focusing public attention upon vinyl chloride, it did create possible problems for the industry.

3. International Labour Office News Release

A News Release from the Washington office of the ILO, announcing an ILO occupational health meeting in Geneva, November 19-28, contained a statement to the effect that vinyl chloride exposures produce emphysema. The Secretary announced that the Washington office of the ILO was unable to provide documentation for this allegation, but had offered to seek such from their consultants. He was asked to procure and distribute the draft report of the Geneva meeting when it becomes available.

4. Status Report on Industrial BIO-TEST Program

Information received by telephone from Mr. Goode indicated that the exposures were continuing on schedule, with no obvious abnormalities in animal behavior or weight gain, or no gross lesions evident. The next quarterly progress report is expected to be received in late December.

CONFIDENTIAL

5. Status Report on TCA Program

Dr. Gaffey has submitted a telephone report indicating that they now have relevant records in hand of about 2,000 employees, and have identified an equal number for whom records are being screened by plant personnel. Their efforts to secure follow-ups on terminated employees through retail credit records have been encouraging. Although there has been some slippage with respect to initial target schedules, they are still confident that the study can be completed by March 1974.

The question was brought up as to whether we should invite Japanese manufacturers of VCM to submit available epidemiological data from their experience. It was the consensus of the group that we should not initiate contacts before the American data has been evaluated, at which time the question could again be considered.

TCA is agreeable to scheduling an oral summary project report in mid- or late-February, preparatory to the drafting of the final written report, and if desired, presentation of a paper at Florence.

6. American Data Presentation at the International Cancer Congress in Florence

The Research Coordinators delegated to the chairman the responsibility for arranging with the Congress administrators for an opportunity to present the available data from the American studies at the Congress, with the option of appointing a small task group to assist him. He is also to discuss this matter with representatives of the European Group to coordinate the two presentations.

7. Dietary Feeding Studies

The Secretary presented a summary of the work being done at the U. S. Department of Agriculture on the micro-encapsulation of vegetable oils as a dairy cattle feed

CONFIDENTIAL

supplement, and suggested that vapor-phase equilibration of the USDA product with vinyl chloride monomer might yield a material suitable for incorporation of the monomer in rat diets. He was asked to try to procure a sample of the gelatin-glutaraldehyde process material for possible evaluation in the laboratories of our members.

Dr. Gehring of The Dow Chemical Company indicated that he believed that the monomer could be fed as an addition to the drinking water, and that Dow was performing feasibility studies.

Interest in an eventual feeding study remains strong; further action will be influenced by FDA action on the SPI petition referred to in the next item of these minutes.

Dr. Rinehart was named chairman of a task group to develop a proposed protocol and cost estimates for a two-year feeding study.

8. SPI Petition on Vinyl Chloride Bottles

Copies of the report in the October 22 issue of "Food Chemical News" on the SPI petition opposing the proposed ban on the use of PVC bottles for the packaging of alcoholic beverages, were distributed to those present. The thrust of that petition is that PVC can now be produced that is essentially free from monomer, and that the use of such PVC produces bottles from which no detectable monomer (with analytical procedures sensitive to not more than 50 ppb in the liquor) migrates into the bottle contents.

The Research Coordinators, after review and discussion of the SPI data, agreed that, on the basis of "no detectable residue" of VCM in the bottle contents, the SPI position that the properties of VCM were not pertinent is well taken, and that there is no present obligation on the part of the MCA task group to intercede in the proceedings.

CONFIDENTIAL

9. Studies of VCM Metabolism

Dr. Gehring presented a proposal for studies on the metabolism of vinyl chloride monomer, and distributed summaries of preliminary work completed at Dow. They have demonstrated a dose-related depression in the non-protein bound sulfhydryl of livers of rats exposed to VCM vapors of from 50 to 5,000 ppm. Various metabolic pathways for vinyl chloride that would be consistent with this observation have been postulated.

Dow has indicated its willingness to do a metabolic study in their laboratories for the project sponsors on a cost-reimbursable basis. This would include C¹⁴ tracer studies with the basic work being done in rats, and with a view to eventual confirmation in dogs and perhaps in man.

Dr. Duffield mentioned that some preliminary work in Europe has indicated that most of the small doses of C¹⁴ labeled VCM administered to rats by intubation is excreted unchanged in the urine.

10. Teratogenic Studies

Dr. Duffield presented a brief report of an ICI study in which female rats were exposed to VCM vapors (at levels of 10,000 and 6,000 ppm, five hours per day, five days per week) from the twelfth day after mating to parturition, with an apparent marked decrease in the number of live births compared to the control group. He could not comment on the statistical significance of these results, or speculate as to mechanisms leading to this lowered fertility. He promised to seek more information for us on these points.

Dr. Gehring described studies Dow has been performing on a number of solvents, including several chlorinated solvents. Exposures were at levels of 2½ times the TLV; only chloroform was effective in reducing live births, destroying all embryos at an exposure level of 300 ppm.

CONFIDENTIAL

He proposed that Dow perform similar studies on VCM, and estimated that they could do so at a cost of about \$18,000.

11. Progress Report on European Studies

Dr. Duffield summarized present observations on the European studies. These now cover almost eighteen months of post-exposure history following the one year of vapor exposures. Groups of approximately 70 animals were exposed to 10,000, 6,000, 2,500, 500, 250, and 50 ppm of the monomer. The incidence of tumors in each group, and the numbers of remaining survivors, are indicated in the following table.

Exposure Level (ppm-VCM)	10000	6000	2500	500	250	50	0	2500 ppm Vinyl Acetate
Zymbal Gland Carcinomas	13	5	2	2	0	0	0	0
Liver Carcinomas Angio-sarcomas	6	11	9	7	2	0	0	0
Kidney Carcinomas Nephroblastomas	3	3	6	3	5	0	0	0
Scattered Tumors (no pattern)	5	2	3	2	1	0	0	0
Survivors	0	0	0	1	1	8	12	0

The relatively low incidence of liver, kidney, and "other" tumors in the 10,000 ppm group is presumed to be due to the high early mortality from Zymbal gland tumors. The control group of animals exposed to 2,500 ppm vinyl acetate experienced no tumors, and all have died from other causes.

Another group of animals, started in January 1973, was exposed to the vapors for four months only; otherwise the conditions were comparable to those in the main

CONFIDENTIAL

experiment. This experiment was done to better simulate the fraction of a workers life in which industrial exposures are likely. At this time, one Zymbal gland tumor has been observed in the 10,000 ppm group.

Among other experiments now under way are groups of 120 rats per group, being exposed to concentrations of 200, 150, and 100 ppm in an effort to better define the no-response level. These were started in June 1973 and so far no tumors have been observed.

A group of 60 rats is being exposed to 30,000 ppm in an effort to duplicate Viola's work. No tumors have yet been seen. Exposures began in June. At the same time, Wistar strain rats, and somewhat later, Swiss mice and hamsters were started on a series of exposures ranging from 10,000 ppm and below. No tumors have been observed to date.

12. IBT Pathologist Visit to Dr. Maltoni's Laboratories

The European Group has indicated that late January or early February would be an acceptable time for an IBT project pathologist to visit Dr. Maltoni. It was the consensus of the Research Coordinators that Dr. Callandra would be the best man for such a visit. Dr. Torkelson was delegated the responsibility for making informal contacts with Dr. Callandra to see if he would be available for such a visit. The Secretary was asked to determine from MCA's counsel whether we were free to make a full disclosure to Dr. Callandra of the European data.

13. Studies for Possible Future Support

Among the proposals given serious discussion by the Research Coordinators, the following were identified as the most pressing:

- (1) VCM Metabolic Studies -- \$50,000
- (2) Teratogenic Studies -- \$20,000

CONFIDENTIAL

Dow is to submit proposals on conducting these studies at cost. The Research Coordinators recommend that the TTGVCR be asked to request approval by the Management Group of \$80,000, including contingency funds, for these studies to be begun as soon as possible.

- (3) Prospective Epidemiology -- \$100,000 per year,
indefinitely
- (4) Three Generation Reproduction Studies
- (5) Mutagenicity Studies.

The Secretary was asked to prepare a letter to the TTGVCR soliciting their support, in principle, for the support of items (1) and (2) above, and alerting them to the probable need for the eventual support of the remaining projects.

14. Review of Company Policies on VCM Customer Information

No action was taken on this agenda item.

15. Workplace Surveillance Recommendations

The Research Coordinators recommended that the TTGVCR survey present practices on work area monitoring and analysis, and to collect information on methods and equipment. Personal monitors are of particular interest to the group.

16. Liaison with NIOSH

Concern was expressed that our contacts with Dr. Stokinger and others at NIOSH had not proved to be more effective in maintaining an on-going exchange of information. The Secretary was asked to inquire of MCA officers what should be done at this time to improve the situation.

17. Preparation for Post-Congress Public Information Programs

The Research Coordinators recommended that MCA and

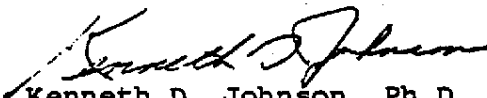
CONFIDENTIAL

the project sponsors give active consideration to potential public relations problems, and to have prepared a non-technical information presentation when industry and Viola data become public at the time of the International Cancer Congress in October. They urged that MCA have a white paper ready for public release, and that the individual companies be prepared to discuss these findings with their unions, their governments, their customers, and the public press.

18. Future Meeting Schedules

It was suggested that the full TTGVCR meet in Chicago on Tuesday, February 19, to receive oral progress reports from IBT and TCA project personnel and to consider the recommendations of the Research Coordinators recorded in these minutes.

Respectfully submitted,



Kenneth D. Johnson, Ph.D.
Secretary
Vinyl Chloride Research
Coordinators

KDJ:mb

Minutes Subject to Approval

December 21, 1973

cc: D. P. Duffield, M.D.
Mr. D. M. Elliott
Dr. Tiziano Garlanda

CONFIDENTIAL

RSV 0000529