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Vinyl Chloride (MCA report)

May 4, 1976

To: T F Minter
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F V Prue
D H Francis
O M Sherman
R W Mendrell ✓

ttached is a report of the meeting of the MC. Vinyl Chloride Technical Panel held April 28, 1976.

Director
Occupational Health Services

C . Johnson, M D.
jap

Att

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Report of MCA--VCM Technical Panel Meeting

The purpose of the meeting was to report the current status of MCA sponsored research projects on VCM and to discuss plans for future efforts.

Dr R A Schwetz - Dow Chemical
Reported on results of study of possible teratogenic effect of VCM.

Concluded that VCM does have some maternal toxicity in animals. The effect was greater in rabbits than in rats and mice. A low incidence of malformations was observed at 2500ppm level in rabbits. This effect was multiplied when ethyl alcohol was given to the animals in addition to the VCM exposure.

Indicated that the study does not lead to the need for great concern for the pregnant female working in plants where VCM levels are not high. Must keep in mind low levels does not necessarily protect against teratogenicity because of possibility of "spike" exposure effect at a critical point in gestation (days 15-35) before the woman knows she is pregnant.

Dr P Watanabe - Dow Chemical
Reported on results of study of metabolism of VCM in animals.

VCM at low intake level (less than 1ppm), majority of the metabolite is excreted in urine; at high intake level (100ppm or more) majority of VCM is excreted in expired air.

Attempt to extrapolate effect of high dose in animal to low dose in man can be very misleading and/or totally erroneous because of the difference in the manner in which the compound similar is handled by the body at the high and low dose levels.

Chemical process for the fate of a chemical in the body:

C ... RH ... RH-H ... Tissue damage
Cancer

Excreted ... Detoxified

Respiration
Urine
Feces
Caveness and tissue

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Dow studies show depression of glutathione levels in the liver correlate very well with tumor (angiosarcoma) incidence in the Maltoni study. Suggests possible dose - response level for VCM may be in area of 50ppm. Question was raised as to possibility of use of high doses of glutathione as a prophylaxis against VCM toxic effect however this is speculative and needs study.

The next step in the metabolism study should be to look at VCM or metabolite binding with DNA and RNA, and also to study in vitro what the primary detoxification reactions are.

Dr M L Kopilmeier - Industrial Biotest
Reviewed animal study procedure and interim reports of results. Now preparing final report. Suggested take close look at survival rates for exposed animals and note dose-time relation in mortality data. Study shows that the incidence of tumors in the animals is dose-related with 30-50% occurring at the 50ppm level. Incidence rate in controls is 4-5%. Peak of dose-response in terms of percent of tumor incidence is at the 200ppm level.

Dr R V Johnston - Dow Chemical
Reported on Dow studies for mutagenetic effect of VCM.

Animal studies (rats only) showed no unusual incidence of abnormal cells at three levels of exposure (50, 200 and 2500ppm) as compared to controls.

Study of cells from human exposed to VCM at levels of 1-5ppm and 1-25ppm showed no increase in chromosomal aberrations as compared to controls. Reported one study in literature of human exposure at "high levels" (specific level not reported) which showed higher aberration rates. Commented on study done by Belikoff, showing increased aberrations in VCM workers. However Dr Johnston stated this study was not fully understood by Dow researchers who had reviewed the data.

Dr William Gaffey - Stanford Research Institute
(formerly with Tabershaw-Cooper Associates)
Reviewed current status of epidemiology study of VCM workers.

Study data now in final stages of analysis.

Data on 9000+ workers in 37 plants.

States cancer incidence seems to be more related to duration of employment rather than latency period and that increasing

maximum level of exposure correlates with increasing mortality rate.

Final report will be available in 3-4 weeks.

Proposals for future research

University of Louisville
number of studies underway or planned - include early diagnosis test evaluation, role of immunological process, metabolism (different approach than Dow study), electron microscopy of tissue, treatment methodology.

Present funding from National Cancer Institute is $2.7 million/year but use is limited to existing methodology.

Proposal that interested MC member companies fund other 5 of 5 studies at cost of $200,000/year plus $50,000/year for contingencies. Information will be sent to companies for review and comment. Consider gift or grant rather than contract. Put no strings on use of money to allow U of L to have flexibility for use of funds in various research products.

Technical panel recommends 1-year grant with review at end of one year and reconsideration for extension.

Additional Metabolism Study
Dow Chemical needs $133,000 for additional year study. This should end all phases of present metabolism study. VCM Technical Panel recommends funding for one year.

Epidemiology study of birth defects
After discussion the panel decided to table plans for this study for the present. May reconsider in future.

Additional discussion
Press release of reports and discussion at meeting of Technical Panel. Panel voted not to make press release.

Panel approved MC sending a letter covering a progress report of MC-VCM studies to appropriate government agencies. Dr Torkelson (Dow , Chairman of Technical Panel, authorized to review and approve this letter.

No specific date was set for next meeting of the Technical Panel.

C J/Jap