



CHEMICAL MANUFACTURERS ASSOCIATION

October 24, 1995

OCT 25 1995

Dear Vinyl Chloride Health Committee Members:

The following items are enclosed:

1. agenda for our October 31, 1995 meeting;
2. Questions for Consideration With Respect to the Proposed University of Louisville Brain Cancer/VCM Case-Control Study. Jonathan Ramlow, Ed Beeler and I plan to meet with Carlo Tamburo in the next several weeks. Please review the list and bring to the meeting any additional questions that you may want to ask of Carlo Tamburo;
3. comments on "Protocol for CMA Vinyl Chloride Mortality Study." Jonathan Ramlow prepared these comments on the AEI protocol based on both Mark Gruenwald's and his own review of the AEI protocol. The comments have been submitted to Ken Mundt of AEI. I have invited Ken Mundt to attend our Committee meeting on October 31, 1995;
4. letter to ATSDR on Vinyl Chloride Protocol, for Combined Inhalation Two-Generation Reproduction and Developmental Toxicity Study in CD Rats. Bill Breslin of Dow Chemical responded to the ATSDR Peer Reviewers' comments and revised the first draft protocol; and,
5. Memorandum of Understanding for Voluntary Research Program Under Section 104 (I) (5) of CERCLA between ATSDR and Halogenated Solvents Industry Alliance, Inc. Please review this MOU prior to the meeting and bring your comments, as ATSDR may propose a similar MOU for the Vinyl Chloride Health Effects research program.

Please call me at (202) 887-1192 if you have any questions. I am looking forward to seeing you at our October 31 meeting.

Sincerely,

Hasmukh Shah
Manager, Vinyl Chloride Panel

Enclosures

SL 108253

3:50 PM 7 Oct 97

CHEMICAL MANUFACTURERS ASSOCIATION
Vinyl Chloride Health Committee
Tentative Agenda

DATE: October 31, 1995
TIME: 10:30 a.m.
PLACE: CMA Offices
2501 M Street, NW
Washington, D.C. 20037

1.0 Discussion of Brain Cancer Case Control Study

- 1.1 Carlo Tamburo (University of Louisville) Proposal
- 1.2 Cost (~~\$10,000~~ to \$150,000)

2.0 Status Report on CMA Vinyl Chloride Epidemiology Study Update

- 2.1 Applied Epidemiology, Inc. - Efforts To Date
- 2.2 ENSR - Contracted Obligations and Problems
- 2.3 CMA - Efforts and Actions To Date
- 2.4 Impact on AEI Contract - Timetable and Financial
- 2.5 Decision on Extending the Update Through 1994
- 2.6 Additional Funding Needs *8K to 9K to update '92-'94*

\$1,000,000

3.0 Discussion of ATSDR/EPA Testing Requirements

- 3.1 Developmental/Reproductive Effects Study Protocol *Revised, sent to ATSDR*
- 3.2 Neurotoxicity Testing Needs *May not need to do.*
- 3.3 Review of Memorandum of Understanding Between ATSDR and HSIA
- 3.4 Identification of Laboratories for Requesting Bids for Developmental/
Reproductive Effects Study *~ 650,000*
- 3.5 Expansion of the Developmental/Reproductive Effects Study Protocol to
Include Molecular Research on Vinyl Chloride
- 3.6 Cost Estimates
 - 3.6.1 Developmental/Reproductive Effects Testing *\$650,000*
 - 3.6.2 Neurotoxicity Testing *\$350,000*
 - 3.6.3 Molecular Research *Swenberg \$50,000*
 - 3.6.4 Legal *60,000*
 - 3.6.5 Contingency *10,000*

30,000
\$1,100,000

4.0 Discussion of Vinyl Chloride Risk Assessments

- 4.1 U.S. EPA *will continue in '96 to correct HEAST table ? Chwell RA*
- 4.2 CalEPA - Superfund site, *see what happened with IRIS*
- 4.3 Richard Reitz PB-PK Manuscript *at agency Sal Goodman - Covington & Burling*
Don Evan - CMA in house

5.0 Update on Vinyl Chloride Litigation

*1st Round { Has Shah
Heraldine Cox
Joe Sewell*

2nd Round Carol Stock

*- Plaintiff attorneys are deposing CMA
staff in Nov & Dec*

Cases in LA, TX

SL 108254

Questions For Consideration With Respect To The Proposed University of
Louisville Brain Cancer/VCM Case-Control Study

~ \$100,000

Carlo:

1. What is the current status of your relationship with each of the three companies formerly comprising B.F. Goodrich in Louisville? When you met with the CMA panel earlier this year you said something about "re-establishing a working network with all three companies."
2. What data would you need to get from all three units? Do you anticipate any problems obtaining the necessary data? Are there any other sources of the necessary data that could be accessed if needed?
3. You have described the brain cancer study in terms of "20-year prospective follow-up" and "25-year combined retrospective" evaluation. What periods of time do these cover? How are the data alike and/or different between the two periods of time?
4. Do you still have the peer reviewers' comments on your 1981 paper on ASL and vinyl chloride? If so, could you make them available to us? This would help us understand how other researchers have viewed the methodology that you employed for that paper and would employ for the brain cancer study.
5. What is your best estimate of the maximum number of brain cancer cases that could be available for study, assuming 1) that you could only get tissue for Goodrich employee cases that were hospitalized in the Louisville area; and 2) that you could get tissue from Goodrich employees hospitalized outside the Louisville area as well? This is really a question about what the maximum statistical power of the study is likely to be.
6. Can we develop a firm timetable for initiation and completion of the study?
7. Can we develop line-item breakdowns and prepare a more detailed study budget?
8. Would you consider working with someone like Kenneth Mundt as a co-investigator/co-author, to add some additional epidemiologic expertise to the brain cancer study and to take full advantage of the follow-up data that he will be generating in the industry-wide cohort study?

COMMENTS ON:

"PROTOCOL FOR CMA VINYL CHLORIDE MORTALITY STUDY"

All in all, a very detailed and clearly thought out protocol. Good job, thanks for the tremendous effort that obviously went into this.

Page 6, top: item "Submit draft proposal to EAP members etc." is redundant, already covered in point D.

Page 8, point R: delete "and approval" and alter to read "Submit final report and journal manuscript to Expert Advisory Panel members for final review and comments;" - the EAP does not approve or disapprove the report, per se.

Page 8, point S: alter first sentence to read "Submit final report and journal manuscript to CMA, with rationale given for comments from CMA that were not incorporated into the final report." - Again, CMA does not approve or disapprove the report or the manuscript, but it will be helpful for the record, Ken, if you simply document your reasons for disagreeing with any specific comment from CMA.

Page 9, third bullet point: delete sentence beginning "For example, does the brain cancer excess etc." Also, alter last sentence to read "If so, are these increased risks plausibly linked directly with workplace factors, including exposure to VCM/PVC, or indirectly through increased surveillance?" - I put that last bit in there in light of the Kodak experience.

Page 10, point 5: delete the phrase in parentheses

Page 11, last paragraph: the first sentence could read "While the causal link etc. is not beyond question, the evidence for or against associations between such exposure and other cancers remains inconclusive."

Page 11, last paragraph: the second sentence could read "Animal studies have suggested the existence of associations with other malignancies."

Page 11, last paragraph: suggest alteration to "A number of occupational cohort mortality studies have been completed, but these have yielded inconsistent results with respect to non-ASL malignancy etc."

Page 12, third full paragraph: the first sentence could read ".....whose recent report suggested the need for additional research regarding VCM exposure and lymphatic/hematopoietic system cancers." - the word "vigilance"

Page 22, top: this sentence could read "All data will then be combined in ProQuest for computation of national and regional mortality rates etc." The word "manipulated" has unpleasant connotations, which is too bad because it is otherwise a perfectly good word.

Page 23: the last paragraph is confusing. You refer to "a three point ordinal measure of degree of exposure", but I'm not sure what you mean. If you mean the plant-specific ordinal scale, you need to make the case that it is usable, because I've always understood that it isn't. If it is something that you will derive de novo, then I don't see where it will come from. With respect to the stratification of variables, you might consider saying that this will be done after inspection of the distributions of the variables, rather than specifying cutpoints you may want to change later.

Page 24, confounding: the second sentence could read "Controlling for sex is unnecessary since all of the cohort members are male."

Page 24, confounding: in the discussion of brain cancers in whites vs. blacks, I think you should have a reference for the statement that some occur more often in white males than black males.

Page 25, regional reference rates: as in the previous comment, I think you need a reference for the statement that there is "strong" regional variability for some causes, and you could perhaps give examples.

Page 25, database structure: perhaps alter the sentence to read "To verify these key data in the index file, a computer-generated report will be generated attempting to replicate the figures in Table 8 etc." This would make it similar to the language on the next page.

Page 26, other data issues: we usually indicate that we will omit SMR and CI computations if both observed and expected are less than 2. This gets at the point raised by Dr. Hammond about this, although I don't know if there is a "right" way to approach this issue.

Page 27, first paragraph: you might consider taking out the sentence which includes "....provided a job exposure matrix and standardized work history are available" since it's not clear that they are available, and the sentence is actually descriptive rather than substantive, probably.

Page 27, second paragraph: the first sentence could read "As the SMR represents the ratio of two weighted averages of stratum-specific rates, thus potentially obscuring a true confounding effect of the stratified control variable, etc." Also, can you be more specific about what is an SMR that differs "appreciably" from unity?

Page 39: I think the Fucic A et al., 1995, AJIM reference should have the asterisk.

Jonathan Ramlow
The Dow Chemical Company

SL 108261



CHEMICAL MANUFACTURERS ASSOCIATION

SEP 26 1995

September 25, 1995

Dear Vinyl Chloride Health Committee Members:

Comments from the ATSDR on the developmental/reproductive effects study protocol are enclosed. I will request Bill Breslin of Dow to prepare a revised protocol based on the comments and a response on items that cannot be incorporated in the protocol. I will send you the revised protocol and the response for your review prior to submission to ATSDR.

Sincerely,

Hasmukh Shah
Manager, Vinyl Chloride Health Committee

SL 108262



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Agency for Toxic Substances
and Disease Registry
Atlanta GA 30333
September 19, 1995

Hasmukh C. Shah, Ph.D.
Manager, Vinyl Chloride Panel
Chemical Manufacturers Association
2501 M Street, NW
Washington, DC 20037

Dear Dr. Shah:

This letter is to inform you that the Agency for Toxic Substances and Disease Registry's (ATSDR) peer review of the study protocol, "Vinyl chloride: Combined inhalation two-generation reproduction and developmental toxicity study in CD rats", has been completed. The protocol was submitted by the Chemical Manufacturers Association (CMA) as a candidate to address ATSDR's data needs for vinyl chloride via voluntary research. Enclosed are the comments of the three peer reviewers.

As stated in the 1992 Federal Register notices on procedures for voluntary research, the ATSDR approved study plan and the peer reviewers' comments, among others, will be available for public inspection at the Agency (57 FR 4758 and 57 FR 54160). Therefore, the Agency requests that CMA respond to the peer reviewers' comments and forward the response to ATSDR within three weeks of the date of this letter. Upon approval of your written response, ATSDR and CMA may then choose to move forward with the signing of a Memorandum of Understanding.

The Agency looks forward to continuing dialogue and collaborative research with CMA on vinyl chloride. Please contact me at 404-639-6306 if you have any questions.

Sincerely yours,

William Cibulas, Ph.D.
Chief, Research Implementation Branch
Division of Toxicology

Enclosures

cc:
Dr. Christopher DeRosa
Mr. Caffey Norman

SL 108263