CHEMICAL MANUFACTURERS ASSOCIATION

September 23, 1988

Dear Vinyl Chloride Panel Members:

The conference call tentatively scheduled for September 29 or 30 is cancelled. A new date will be set up after checking with Panel members for maximum participation.

Meanwhile, please review the enclosed September 15 letter from Dr. Bill Gaffey that summarizes his meeting with Dr. Brian Bennett of ICI, England. The background information leading to this meeting was sent to you earlier, but also is enclosed for your ready access.

At our conference call in early October, we will discuss the EHA's interim report that was sent to you earlier and a course of action for resolving discrepancies between the EHA study and the Angiosarcoma Registry.

Sincerely,

Has Shah

Hasmukh C. Shah, Ph.D.
Manager
Vinyl Chloride Program

cc: Vinyl Chloride Research Coordinators

2501 M Street, NW, Washington, DC 20037 202-887-1100 Telex 89617 (CMA WSH)

Monsanto

ENVIRONMENT SAFETY & HEALTH

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

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SPECIAL PROGRAMS DIVISION

From Hao Shah
Ref. No. VC Panel
Date 9/23/88

September 15, 1988

Dr. Hasmukh Shah
CMA
2501 M St. NW
Washington, DC 20037

Dear Has:

Dr. Bennett and I went through the Registry cases and the EHA cases, but I realized afterwards that we hadn't really come up with any specific things that could be done to resolve the remaining inconsistencies. Therefore I went through the data and rearranged the results somewhat. The net results are pretty much what Richard Doll found, but with some specific things that might be done.

The Registry includes 29 cases (all deaths) that occurred in U.S. workers up to the closing date of the EHA study, and these are potentially eligible for inclusion in that study. The EHA study lists 37 liver and biliary cancer deaths, using death certificate diagnosis, 15 of which are ASL. One of the Registry cases, No. 24, is in fact a cholangiosarcoma. It appears to be EHA Case No. 36 (listed by EHA as non-ASL) although the beginning date of exposure differs by 2 years in the two lists. I omit this case in what follows, so that we have 28 Registry cases and 36 EHA cases.

I matched the two lists using date of birth, date of first VC exposure and date of death, which were common to the two lists. I considered a Registry case and an EHA case to be the same if each of the three items agreed within a year, with one exception. There were 20 matches, as Doll says.

Registry No.	EHA No.	"A" means EHA called death an ASL
01	25	A
02	20	
03	26	A
04*	23	
05	22	A
06	27	A
07	15	A
11	08	
13	10	A
16	18	A
17	28	A
19	37	
21	35	
22	19	A
26	17	A
27	11	A
28	13	A
29	31	A
30	01	
31	12	A

*Birth and death dates matched exactly, but first exposure began in 1952 in the Registry and 1949 in EHA.

The above list tells us 3 things. First, there are 8 Registry cases for which there are no apparent matches in the EHA listing. These are Registry numbers (08, 09, 10, 12, 18, 20, 23, 32). (Case 32 actually matched EHA's Case 31 but the former is the only Monsanto case while the latter is one of 13 from the same factory, so the match cannot be correct.)

Second, there are 16 EHA cases (02, 03, 04, 05, 06, 07, 09, 14, 16, 21, 24, 29, 30, 32, 33, 34) that are not in the Registry, Case 07 is ASL according to the death certificate. This agrees with Doll's figures.

Third, EHA cases (01, 08, 20, 23, 35, 37) were actually ASL deaths although the death certificate did not so state. This is true because they were in the Registry and therefore histologically confirmed by that source.

Therefore as of our present state of knowledge 20 of the 28 Registry cases were actually found by EHA, but not all of them were identified as such because the death certificates did not all mention ASL.

This leaves two questions. First, where are the remaining 8 Registry cases? Second, are there any new ASL deaths among the 16 EHA deaths that were not in the Registry? (EHA case 07, for example).

Of the Registry cases, names are missing for 4. It is possible that these could be obtained from the companies involved (Goodyear and Great American). It seems to me that Otto could search the EHA cohort to see if he could match them with cohort members.

Depending on the results we would conclude that (a) they were included but the death certificate cause was something other than ASL (b) they were included but were counted as alive or lost to follow-up or the death certificate was not found, or (c) they were not included in the original VC study either by accident or design. Of course, in the last case it could also be true that the identifying information was wrong in one or both of the two sources.

The second question may not be answerable. Those 16 deaths are among the 37 that EHA is trying to verify, and that effort may not be successful.

I think we have squeezed all of the information out of the Registry and the EHA study that can be obtained without further date from Otto.

Yours sincerely,

William R. Gaffey, Ph.D.
Epidemiology Director

/jf

IMPERIAL CANCER RESEARCH FUND

Cancer Epidemiology and Clinical Trials Unit

UNIVERSITY OF OXFORD

Acting Director: Emeritus Professor Sir Richard Doll, D.M., F.R.S.
Telephone: (0865) 53762

Gibson Building
The Radcliffe Infirmary
Oxford OX2 6HE

22 December 1987

RD/CH

Dr G.M. Paddle,
Imperial Chemical Industries PLC,
Epidemiology Unit,
Alderley Park,
Macclesfield,
Cheshire SK10 4TJ.

Dear Gerhard

I am sorry not to have replied to your letter of 20.10.87 before but it needed detailed attention and I was very hard pressed to complete a major report for NRPB on the UK atom bomb participants which had to be completed by a fixed date.

I have now had time to think about Dr ten Berge's letter. He has a good point. I agree that only 20 of the 37 liver cancer cases causing death in the EHA study are in the Registry as having caused death before 31.12.82 whereas there should have been 29 (though I disagree with one of his numbers - I identified no. 31 in the Registry and failed to identify no. 29). Approximately 6 deaths from liver and gall-bladder cancer were expected so that that that leaves approximately 11 deaths that are either angiosarcomas missed by the Registry, excess liver (or gall-bladder) deaths other than angiosarcoma, or an excess number of misdiagnoses. Any of these might be the true explanation, but meanwhile my confident conclusion that the only tumour of the liver produced by vinyl chloride is angiosarcoma is weakened. Nevertheless the fit with the British, Canadian, and Italian data makes me still put my money on its truth - in which case a fair proportion of the 11 extra deaths must be angiosarcomas not picked up by the registry. This would be an important conclusion and makes it worth your trying to discover what the EHA liver cancer deaths actually were (nos. 2, 3, 4, 5, 6, 7, 9, 14, 16, 21, 24, 29, 30, 32, 33, and 34). Two of them could conceivably be in the Registry with some wrong information (i.e. 9 Registry no. 32 and 37 Registry no. 19) but I doubt if they are.

The other things we want to know are whether: (i) the missing Registry cases came from companies that did not participate in the EHA study (which might account for Registry numbers 12 (though it seems unlikely that Firestone didn't) 23 (Great American Chemical Co.) and 32 (Monsanto), and (ii) what were the certified causes of death of men who presumably should have been in the EHA study and (if liver or gall-bladder cancer) why weren't they there: namely 08, 10, 18, 19, 20, and 23 (and 12, 23, and 32 if the relevant companies were included).

Is there any chance of your obtaining any of this information?

With best wishes for the New Year,

Yours ever

Richard Doll

MINUUT

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afschrift

Imperial Chemical Industries
Epidemiology Unit
Dr. G.M. Paddle
Alderley Park, Macclesfield
Cheshire, SK10 4TJ
Engeland

W. ten Berge, CVMD Ms 2

O 658/87 CVMD 10.9.1987

Dear Geoffrey,

Thank you for sending me your letter to Sir Richard Doll and his answer to you. From the answer of Doll I got the feeling that he had not understood completely my question. Therefore I want to make again my point clear to you.
For that purpose I send you:

- a copy of the list of liver cancers (table 17) of the US-epidemiologic study on VC-exposed workers of Environmental Health Associates (EHA).
- a copy of the list of US-ASL-deaths from the ASL-Registry of Dr. Bennett.

The end of follow-up of the EHA-study was December 31, 1982. Up to that date 32 US-ASL-deaths were recorded in the ASL-Registry. Number 14, 15 and 25 were removed from the Registry, because they were not confirmed ASL-cases. So in table 17 of the EHA-study 29 of the 37 liver cancers should be due to ASL.
To confirm this I tried to match the dates of birth, of death, of start and of termination of employment etc. of the US-ASL-deaths from the Registry with the same dates of liver cancer deaths (table 17) of the EHA-study.

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However, matching failed for the following US-ASL-deaths from the Registry: 8, 9, 10, 12, 18, 19, 20, 23, 29.
Possible causes may be:
- Not all polymerization plants with US-ASL-deaths were included in the EHA-study.
- Wrong figures in the EHA-study as Sir Doll proposes.
- Confirmed US-ASL-cases in the Registry were not as liver cancer recorded on the death certificates. This would suggest still more liver cancers?

Shortly this is my problem. I have no further information to solve this. I would highly appreciate your help for clearing these findings.

Kind regards,

Central Department for Safety- and Environmental Matters,

Wil ten Berge

1 Enclosure