LIED CHEMICAL CORPORAT

MEMORANDUM

November 20, 1972

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MEMO TO: Mr. J. C. Fedoruk
Mr. A. P. McGuire

FROM: W. A. Knapp

There was considerable confusion at this meeting as to agreement to retain confidentiality of the data. When Dr. Harris arrived in Italy, it was discovered that Mr. Best's (MCA) agreement with Mr. Lindsell (ICI, Director of European Monomer Group) was not satisfactory. Consequently, Dr. Harris was shown the equipment and given only the test protocol, not the results. The protocol is attached.

At our meeting, a few wanted limitations placed on confidentiality (particularly as it may relate to disclosure requirements in Food Additive petitions) but most thought disclosure restrictions a detail, difficulties concerning which were very unlikely to occur. After rather weak reassurances, Mr. Don M. Elliot (ICI) decided that he would take it upon himself to disclose what he knew. He requested that no notes be taken (which request was honored) so that summary of results attached may be subject to some inaccuracies but is generally correct. Further, with respect to confidentiality of data, it is reported that a Dr. Caputo at the Univ. of Florence (a cohort of Dr. Viola?) will present a continuation of Dr. Viola's results at a meeting in 1974 which will thereby reduce confidentiality of results. Apparently, Dr. Viola's presentation at Houston about 2 years ago was made without Solvay's permission that Europeans are very sensitive about disclosure conditions.

The major disclosure is that substantial numbers of tumors were formed at 10,000 ppm and single tumors at concentrations as low as 500 and 250 ppm. It is to be noted that exposures were for one year and are now completed except where replacements were made for early deaths. How many such replacements were necessary was not clear. The fact is exposures have been completed and animals are now being retained awaiting death from whatever cause. One thing not clear in the protocol is whether food and water for the

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animals remained in the cage during the exposure period; the animals were apparently not removed from exposure chambers between exposures. It is the feeling of the writer that absorption on fur and subsequent licking plus solution of gas in water or in fat component of food can be the greatest source of intake and must be monitored if results are to be meaningful. Many questions with respect to protocol and results could not be answered.

To the most knowledgeable people, the results were sufficiently disconcerting to prompt immediate reconsideration of the U.S. Industry Program. Accordingly, the Task Force was to meet directly following our session. Among things to be reconsidered are metabolism studies and the epidemiology deleted from first program because of cost.

Recipients of this memorandum are reminded that by agreement with the European Group, we will exert every reasonable effort to retain contents in strict confidence within company personnel. To this end, it is requested that disclosure not be made beyond recipients of this memorandum without prior notice to the writer. Only this will reasonably retain the strict confidentiality required.

W. A. Knapp

WAK:md

cc: Mr. W. S. Ferguson
Mr. H. L. Noble
Mr. S. R. Stevinson

Vinyl Chloride Monomer - European Project Protocol

Animal species: Sprague-Dawley rats of thoroughly documented pedigree especially with regard to cancer incidence in various tissues.

Dosages: 10,000, 6,000, 2,500, 500, 250, and 50ppm. 65-95 animals per group.

Time of exposure: 4 hours real time/day, 5 days per week for one year. Animals are observed until natural death. Professor Maltoni feels that one year is better than longer exposure since toxicity may kill animals before cancer develops especially at higher dosages.

Animal housing and handling: All animals of one group were in one chamber which had three levels with two cages of 10 or more animals each at the beginning of the experiment. Of the original 577 animals at the start of exposure, 275 have died of natural causes. There is a separate mixing device for each chamber. The VC air mixture is fed through a large pipe into each of the three levels of the chambers. A gas sample tube leads from each metering device to a central gas chromatograph. Periodic samples are also taken from the chambers to maintain the dosage very close to the desired levels. Records are complete and neat. Professor Maltoni is intimately acquainted with every phase of the work. Three Ph. D's work on this phase of the work. A standard balanced laboratory is supplied by a feed company according to his formula.

Observation and pathology:
Weighed every two weeks.
Observed individually several times daily.
Careful clinical examinations weekly.
On death complete autopsy. Those with tumors are x-rayed-whole body by a special technique which shows cancerous tissue. All organs examined carefully. Professor Maltoni personally reads all slides. Color photos are made of tumors.

European Project Sponsors:
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Solvay et Cie
La Cellophane
Montedison
Rhone-Progil

Research Investigator in charge:
Professor Cesare Maltoni
Instituto Di Ancologia
Bologna, Italy

Vinyl Chloride Monomer

Inhalation Study

	Conc.(ppm)	No. at start/ surv.	G*	K*	L*
Vinyl acetate	2,500	-	-	-	-
Vinyl chloride	10,000	95/22	7/3+1m	2	
	6,000	70/30	3/1+1m	-	
	2,500	70/45	0	4	
	500	70/50	1+1m?	-	
	250	70/50	1	-	
	50	70/50	0	-	
	0	70/50	0	-	

8 (total), do n remember distrib.

Exposure 4 hrs/day, 5 days/wk for one year; animals now 72 wks. old. Gross and microscopic autopsy made as animals die.

G* - ceruminosa gland in ear

K* - kidney

L* - liver