



Air Products and Chemicals
INC

CHEMICALS GROUP

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747

April 6, 1976

Mr. J. R. Smith
Special Studies Staff
Environmental Protection Agency
National Environmental Research Center
Research Triangle Park, North Carolina 27711

Dear Mr. Smith:

This will furnish you further information on the subject of reported non-polymerization worker cases of angiosarcoma which we discussed by telephone on March 31 and April 2.

Some confusion seems to have arisen over the nomenclature applied to the reported cases of angiosarcoma in Connecticut. They have been variously called "community cases" or "neighborhood cases" in the media, in EPA documents (STAR Document, p. 1), and in the EPA hearing (cross-examination of Barry Castleman by Dr. William Marcus, hearing transcript p. 42, copy attached), "non-polymerization cases" by NIOSH, and "non-occupational cases" by CDC and in other places. Unfortunately, we seem to have added to the confusion by using both "non-occupational" and "non-polymerization" on page 19 of the Air Products' submittal to Dr. Goodwin, dated February 23, 1976.

I will hereinafter use the NIOSH designation of "non-polymerization" for employees not working in PVC plants and "non-occupational" for persons not employed in any part of the PVC industry.

The cases with which we are concerned are therefore "non-polymerization" cases. NIOSH does list these in "Table II" which they maintain. The latest listing of these cases is dated September 12, 1976, and is attached. It has not been distributed routinely with Table I over the last few months, and Drs. Adams and Smith of this company were informed earlier this year by Dr. Lloyd that it had been discontinued. This led to the statement in the submittals by Air Products and the Society for the Plastics Industry that these cases had been dropped. In a conversation today with Dr. Pierre Decaufle of NIOSH, he confirmed that this list is not normally distributed now, but that it is still in existence and will be maintained.

The burden of proof is on NIOSH to substantiate their listing of these cases, and to show their relationship to vinyl chloride. No one presently exercises this responsibility. Angiosarcomas do occur in populations not exposed to vinyl chloride. The CDC has recently published a survey of ten cases in Wisconsin which have no vinyl chloride relationship whatsoever (copy attached). The Connecticut cases would seem to fall into a similar classification except for the very casual relationship to fabrication operations. This type of correspondence is expected to occur on a statistical basis from time to time.

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Regarding the foreign cases listed in NIOSH Table II, Germany 03 filled aerosol cans where the exposure from leakage was reported to be high. We have no more information than NIOSH on Germany 07, or Great Britain 02. Italy 01 did not have primary liver angiosarcoma. Sweden 02 worked in an obsolete acetylene-process vinyl chloride plant where the exposure was high.

The two U. S. (Connecticut) cases are discussed by you in the footnotes to Table 6-19 of the STAR Document, where you quote Dr. L. B. Thomas of the National Cancer Institute. He states that both cases are uncertain. Furthermore, EPA has stated that their measurements of vinyl chloride around fabrication plants show it to be "almost negligible" (Preamble to Standard 40 FR 59534). The highest found was 6 ppb, and none was found at 3 of the 5 plants tested. Thus, these "non-polymerization" cases are doubtful in relationship to vinyl chloride, and do not support any concern for harm at "levels of exposure as low as 1-10 ppm" (STAR Document, p. 1).

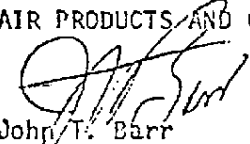
The exchange between Mr. Castleman and Dr. Marcus at the EPA hearing indicates that the EPA has reached the same conclusion. This is supported by the statement in Appendix E, page 5, of the Risk Assessment Document by A. M. Kusmak and R. E. McGaughey that, "This survey has produced no evidence that living around vinyl chloride plants is a risk factor in the occurrence of liver angiosarcoma."

Thus, we stand on our position that there is no demonstrated risk to persons not exposed to high concentrations of vinyl chloride for long periods of time, and therefore the proposed standard is unnecessary.

I hope that this clarification is of help to you, and apologize for any confusion to which we may have contributed. We will be happy to discuss any other part of our comments with you whenever you may wish.

Very truly yours,

AIR PRODUCTS AND CHEMICALS, INC.


John T. Barr
Technical Manager

JTB:mjv

Attachments

cc: Mr. G. Baise, Ruckelshaus, Beveridge, Fairbanks & Diamond, Wash., DC
Dr. D. R. Goodwin, EPA, Research Triangle Park, NC
Mr. J. Hadley, Keller & Heckman, Wash, DC
Mr. R. Harding, SPI, New York, NY

bcc: A. R. Adams
R. Fleming
R. H. Schonck
W. M. Smith
L. B. Tenner

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1 DR. MARCUS: Do you know of any evidence of the
2 increased risk in the general population, other than the
3 studies that have been done in work?

4 MR. CASTLEMAN: Aside from the fact that there
5 were apparently two neighborhood cases with no known
6 occupational exposure, no I don't.

7 DR. MARCUS: I would like to say that EPA
8 investigated very carefully those cases, and we consulted
9 with our expert doctor, Hans Popper of Mount Sinai, and
10 it was his expert opinion that these people did have
11 angiosarcoma; that was of a different type than that caused
12 by vinyl chloride monomer, and I must say, to date we
13 do not have any evidence that angiosarcoma has been
14 produced by vinyl chloride monomer in the general population.

15 MR. CASTLEMAN: I think it is important to
16 realize that only about one-fourth of the present PVC
17 plants were operating 20 years ago. The latency of this
18 disease is 20 years or more, and of these ten plants,
19 at least one-fourth of the present level of plants, which
20 is about ten, the total production rate is one-tenth of the
21 rate it is today. The population may also have been thinner
22 around the plants than it is today.

23 So, if you look at the present situation in terms
24 of how many people lived near the plants of a certain
25 size, it bears little resemblance to the situation 20

1 years ago.

2 The mortality experience that we observe today
3 started 20 years ago. I don't think the absence of
4 cases is any proof of anything. Wouldn't you agree with
5 that?

6 DR. MARCUS: In general I would say that is a
7 very cogent comment. The only thing here is that vinyl
8 chloride happens to offer us a unique opportunity to
9 see an extremely rare cancer, which we can say is maybe
10 due to the substance in question, rather than an increased
11 rate of cancer, which is a very difficult thing to assess.

12 That is why I say, I was hoping somebody would
13 have some information about VCM induced angiosarcoma in
14 the general public, because we have not been able to find
15 it as yet.

16 MR. CASTLEMAN: I talk to the same people you do

17 CHAIRMAN DENNEY: Dr. McGaughy.

18 DR. MC GAUGHY: I just have one short question.

19 We are interested in getting as accurate a
20 picture as we can as to what the risk is to the population
21 due to vinyl chloride exposure. You mentioned there
22 were two or three factors that we have not considered.

23 Mainly the carcinogenicity of vinyl chloride and
24 other chemicals and the transplacental effects that might
25 caused to expectant mothers.

NIOSH
September 12, 1975

TABLE II

REPORTED CASES OF ANGIOSARCOMA OF THE LIVER AMONG
NON-POLYMERIZATION WORKERS EXPOSED TO VINYL CHLORIDE

COUNTRY	CASE #	BIRTH DATE	1st VC or PVC EXPOSURE	DX ANGIO-SARCOMA	AGE AT DX	YRS 1st EXP TO DX	TOT YRS EXP	DATE OF DEATH	
Fed. Rep. Germany	03*	07-16-30	06-09-52	03-00-73	43	21	14	10-10-73	Note 6
Fed. Rep. Germany	07*	05-09-36	00-00-60	00-00-74	38	14	03	12-16-74	Note 9
Great Britain	02*	09-08-14	00-00-46	02-00-70	55	24	11	12-00-70	Note 1
Italy	01	06-15-34	00-00-65	04-19-71	36	6	3	04-16-71	Note 2 & 7
Sweden	02*	11-27-11	00-00-45	05-15-72	61	27	23	08-16-72	Note 3
United States	14	00-00-13	08-18-38	06-00-73	60	36	00	07-03-73	Note 4 & 8
United States	15*	00-00-25	00-00-00	07-00-72	47	00	00	02-15-73	Note 5

Note 1 Pouring PVC oil mixture onto fabric bases

Note 2 Production of PVC sacks

Note 3 Production of Vinyl Chloride

Note 4 Machine operator covering electrical wire with PVC plastic insulation

Note 5 Accountant at plant making PVC fabric

Note 6 Loading pesticide cans with VC propellant

Note 7 Angiosarcoma involving liver, lung, and pericardium. Although difficult to determine, primary site seems to be pericardium.

Note 8 Diagnosis: Sarcoma (possibly "angiosarcoma"), liver. Possibility of generalized neoplasm of the reticuloendothelial cell system cannot be ruled out.

Note 9 Assistant Factory Chemist

* Indicates microscopically confirmed angiosarcoma of the liver.

"00" Indicates unknown data.

AP00048811

MEDICHEM 4TH INTERNATIONAL CONFERENCE

HAIFA, ISRAEL

7-10 SEPTEMBER, 1976

Institutional Interactions in Problems of Occupational Health:

An Industry View on the Lessons from Vinyl Chloride

by

A W Earnes
ICI Plastics Division

AP00048812

Institutional Interactions in Problems of Occupational Health:
An Industry View on the Lessons from Vinyl Chloride

A W Barnes

I have been asked to speak this morning about "Institutional interactions in problems of occupational health". The views I want to express are personal ones: they derive solely from my personal experiences over the past 2½ years when I was closely involved with the vinyl chloride problem. My involvement, and that of my colleagues in the general management of the European PVC industry, was in part as a layman in a highly specialised field where the initial contributions had to be made by experts and professional people from universities, government and research associations. As industrial general managers, and with our trade union colleagues, our prime responsibility was to see that all possible steps were taken at the maximum speed to ensure the safety of the plant workers: ultimately though I believe we also made some contribution through our experience in bringing together the views of experts in different specialist fields, because, as generalists, the critical appraisal and pulling together of expert opinion is part of our normal daily jobs. Once our colleagues outside industry had found that our objective was precisely similar to theirs - i.e. the full safety of our workers - the result was an enormously fruitful co-operative effort involving everyone who could help. Indeed, if it were not for the personal tragedies which preceded and initiated all this effort, we would have good reason for feeling entirely pleased with the way groups of people from different disciplines and countries, from different institutions and with different responsibilities, came together to solve an immensely difficult problem.

Of course we had our difficulties in the early days. Industry seems nowadays automatically to be cast in the role of the villain of the piece by much of the media, and a suspicion that this might be true exists in the minds even of reasonable people. Our first task therefore was to convince people that we were just as concerned as they - perhaps more so - to see that our staff worked under safe conditions: but this was not too difficult since the statement was true, and the people we were involved with in government, universities and trade unions were willing to listen, and then to observe that our actions confirmed our words.

Another difficulty initially was the belief that this was a medical problem and that only doctors therefore could speak with authority, even when it came to framing legislation. But a doctor is not a lawyer nor yet an engineer: nor is he an expert on industrial control processes or analytical techniques; and rarely do we find, in any one doctor, an expert epidemiologist, toxicologist, oncologist, clinician and statistician combined! Yet all these and many other disciplines were necessary for the definition of the problem and for its resolution; and some of these resources industry could provide. The barriers between the medical profession and industry were real and potent because they prevented, initially, the dialogue which alone could lead to a full understanding of the situation: but with goodwill they were broken down and have led, I believe, to enhanced mutual respect and indeed to many lasting friendships.

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One of the bigger problems, which persisted throughout the period, was the effect of reports and comment from American sources. The character of some of these came as a total surprise and one of the major lessons many of us learnt from the vinyl chloride problem was that American information had to be treated with extreme care. America is enormously important because of its resources, and its influence throughout the world; but its method of debating matters of public concern is very different from the custom in Europe. The glare of publicity which attends these debates certainly seems to encourage some scientists to speak out with a certainty that is hardly justified by the quality of their information. Whatever the reasons, many American reports were of doubtful validity because they frequently gave information which was incomplete or unconfirmed or simply inadequately analysed. Their impact nevertheless was major: by heightening the feeling of alarm, they increased the pressure on European institutions to take up extreme positions, as in the USA, and this, if it had happened, would have made co-operation and rational analysis extremely difficult. Fortunately it didn't happen: medical institutes, government departments, trade unions and industry realised that, while taking full note of US information and comment, their proper task was to develop a European response, independently, to the problem. In this context it is interesting to note a remark by Dr Marcus Key, who was director of NIOSH at the height of the vinyl chloride crisis. Speaking at the Royal Society of Medicine Conference in September 1975 he commented that in Europe we seemed to have reached roughly the same end point as the USA without the tensions and trauma surrounding the generation of the OSHA regulations.

How did we achieve this, first nationally and then internationally in Europe; and how did representatives of institutions from many different nationalities and with widely different interests and experience learn to work together? At the national level, I can speak more knowledgeably of the UK, although similar processes, I know, developed in the rest of Europe.

At an early stage in the UK, the government set up a Tripartite Working Group composed of senior representatives from government, the trade unions and industry. It is important to note that, at no point, did this become a negotiating body made up of three factions. From the beginning, it was one group with a single common purpose: it owned the problem as a group and it was committed, as a group, to the solutions it developed. This attitude is well exemplified by one of its actions: a smaller tripartite group was formed from the main committee to visit all the UK PVC plants. The purpose of this was not to check that management was doing the right things - though we had the opportunity of seeing this too - but to allow everyone on the plant, from works manager to plant operator, the opportunity of checking that we, who ultimately had to recommend standards and codes of practice, were doing our job properly. On each visit an open forum was held to allow the works staff to fire questions at us so that they could determine to their own satisfaction that we knew what we were talking about. The standard of debate and of information throughout was at an extremely high level: and a very important result of the visits, was that the tripartite group and the workforce throughout the industry were very firmly united in a common endeavour.

Internationally, the European PVC industry formed a series of vinyl chloride committees under the auspices of CEPIC (the European Council of Chemical Manufacturers Federations); and within these committees a great deal of co-operative work was done in both the technical and medical fields. As a

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result of this, representatives of the main committee were able to speak with authority for the whole of Europe whenever a contribution from industry was required. This was no mean achievement, for Badische and ICI and Solvay and Montedison are just as much institutions in their own right as is the University of Louvain or the University of Wurzburg or the Mario Negri Institute.

But one of the most constructive of European moves was the invitation to CEFIC from Directorate General V of the Commission to join with their Ad-Hoc Committee on MAK values in considering and advising on a possible Commission directive. This committee was composed largely of distinguished medical academics and the meetings provided the first opportunity for a dialogue between European industry and the European medical establishment as well as with the Commission itself. Of course there were some misunderstandings initially, for industry was talking the language of science and technology while our colleagues were talking the language of medicine. As an example may I quote the initial belief among our medical and commission colleagues that if a directive were to lay down a maximum of, say, 10 ppm (averaged over any 8-hour period) then industry would be able to operate at a constant level of 9.5 ppm. They had not appreciated that the products of industrial processes are rarely constant day in and day out, and that there is always a variation about a mean. Because of this, for 10 ppm never to be exceeded, plants must be operated, on average, well below 5 ppm and will frequently be producing results of 1 or 2 ppm! So a legal requirement for 10 ppm not to be exceeded, is very close to a medical requirement that average exposure should be below 5 ppm!

Fundamental difficulties of this type were relatively quickly sorted out however because of the willingness of members of the committee to meet and discuss the problems on an individual basis. For instance, Professor Maltoni from Italy and Professor Lauwerys from Belgium paid day-long visits to ICI's plants in the UK and Professor Foa arranged for one of his Italian colleagues to visit us also. Similar exchanges occurred in the other countries of Europe and, quite soon, we were all talking a common scientific language and progress was rapid.

Within DGVI of the Commission initial progress was not quite so positive. This Directorate-General, which was concerned with the control of PVC for packaging foodstuffs, also remitted the problem to its scientific advisory committee but unlike DGV made no formal invitation to industry, or other interested parties, to contribute. The committee, composed largely of toxicologists, had the impossible task of proposing control levels for vinyl chloride in foodstuffs, where the human exposure levels were already a million times lower than any level at which carcinogenic effects had been observed. Not surprisingly, their conclusions could owe little to toxicological data; and in an understandable effort to ensure the absolute maximum in safety while still, they believed, supplying a practicable solution, their first proposal was that "vinyl chloride should not be detectable in food or potable water by an agreed method. Attempts should be made to develop generally applicable analytical methods with a sensitivity of the order of 0.001-0.002 mg/kg."

An obvious philosophical objection to this early proposal was that it related the control level simply to the state of advancement of analytical science which of course is in no way related to the question of hazard from vinyl chloride. Of even more concern to industry, though, was that

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it was a totally impracticable solution since the problem of variation of results about a mean had again been overlooked; and the problem here was complicated further since vinyl chloride reaches a foodstuff by a slow diffusion process. In addition to the normal variation in any industrial process, which is to a degree controllable, a further factor therefore is the period of storage of the product, which is not. To ensure a non-detectable amount in any foodstuff at any time, it would be necessary to control at the factory or packing station at a level say of 1/10th of non-detectable! A moment's reflection will make it clear that this is somewhat difficult to measure! - and therefore impossible to ensure. Effective control of an industrial process demands the facility to measure key parameters of the system while they are still within specification, so that any trend away from the norm and towards the specification limit can be detected and then corrected.

Our concern, within industry, was such that the CEFIC committee produced a discussion paper which some of you may have seen. It is the only document I know which attempts to bring together, in an orderly fashion, all the facts and factors relevant to a particular aspect of the vinyl chloride story. Its purpose was to encourage debate on matters of judgement and, if necessary, to allow argument in areas of disagreement - but always disciplined by facts and figures. I believe it has proved of some value and that in this part of the vinyl chloride problem - as in that concerned with worker protection - real progress became possible once we had found a way for medical experts, government representatives and industry, to challenge and to educate one another in rational debate.

These are but a few examples of how, in Europe, we learnt to work together. In all they add up to a story of some considerable success: but before we get too complacent I think we have to ask the question "Did we do - have we done - all we could?". I'd like to spend the rest of this paper in explaining, as a layman in a medical field, why I believe we have not.

It seems to me that vinyl chloride is almost unique among known human carcinogens. Our knowledge of its effects on animals, through the distinguished researches of Professor Maltoni, is more extensive than for many, perhaps most, other carcinogens; and our knowledge of its effect on humans, because of the rarity of angiosarcoma of the liver, is in almost all cases precise and unambiguous. It must be rare to find so clear-cut an effect on a human population in conjunction with such thorough animal experimentation. I would have expected that the data on vinyl chloride would have been seized upon to see what more it could teach us about carcinogenesis in general. But what we have had is a flood of papers on epidemiology by epidemiologists, on toxicity by toxicologists and on metabolism, clinical treatment, immunology, chromosome aberration, etc. Any attempt at analysis of the human data on a world scale has been minimal and most references to Professor Maltoni's work have been limited to a superficial treatment of the results from his experiment BT1. It is indeed startling to observe that, from all of Professor Maltoni's massive research, the only conclusion that has actually been used in the field of industrial hygiene is the conclusion that vinyl chloride is a carcinogen. As an employee of one of the companies who sponsored Maltoni's work, I feel bound to ask whether the cost and effort, on our part and on his, was worthwhile if this is the only useful information we can extract.

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Why has the yield been so poor? Could it be that the medical profession itself is getting a little over-specialised and that vinyl chloride has been seized upon by the specialist as a useful vehicle for testing out theories and advancing knowledge in his own specialism? Is it possible that rather more interaction is required within the medical profession and that we need the interest of one or two good medical "generalists" who can pull together all the data and begin to answer some of the outstanding questions? Only you can say whether these are foolish questions or whether they are worthy of some consideration. But the fact remains that there are questions still to be answered.

General to the whole problem of carcinogenesis and toxicity is the relationship between the results of animal testing and the effect of the toxic substance on humans. How many times in the past 23 years have I heard the remark that we don't know how to relate the one to the other; and while we remain in this ignorance the value of work like Professor Maltoni's is diminished. I cannot help feeling some surprise that there has been so little effort to analyse the human data on vinyl chloride and to relate this to Professor Maltoni's comprehensive findings. Of course any relationship we find for vinyl chloride will not provide the key for all future problems but it would at least be one more step along the road of understanding.

There remain two major questions, specific to vinyl chloride, which demand more application by all of us. The first asks whether there remains any risk to the consumer from food, wrapped in PVC, at the infinitesimally small levels of vinyl chloride which can still be detected: and if so, what the level of risk is. The problem for toxicologists is that there is no experimental animal data on vinyl chloride at the minute exposure levels we are talking about: but even if there could be, they would still be faced with the problem of relating rats to humans and this is a permanently insoluble problem if we confine our studies to evidence from ingestion. There would be no possibility of obtaining convincing human ingestion data even if the risk were a significant one - which is of course completely contrary to our belief. Yet, tantalisingly, there exists a great deal of data on the effect of inhaled vinyl chloride, on both rats and humans, which, as I've already indicated, could give us some pointers to the relative sensitivities of the two species. The need is to achieve some definition, albeit imprecise, of a risk; for in matters of public concern qualitative generalities have little - or too much - impact depending on the speaker. The problem is to find some way of bringing all the results together to bear upon the question.

Within industry, we were greatly indebted to my colleague Dr K S Williamson who pointed out that all known results, inhalation, ingestion, human and animal, could be examined in one table by defining exposures in mgm/kgm of body weight; and that, when this was done, a degree of consistency could be observed across all the results. Starting from these unified results, and with the help of published work by Schneiderman, Mantel and Bryan and the late Dr Leo Friedman (this last incidentally in a very relevant WHO report which has received surprisingly little attention) the CERIC discussion document was able to suggest a value for the maximum residual risk from foodstuffs of the order of 1×10^{-10} , or some 80,000 times lower than the risk, calculated by Friedman, arising from the consumption of 70 gms of "charcoal-broiled" steak daily. The analysis we have done is an elementary and quite unsophisticated one: our answer is certainly imprecise - how could it be otherwise at these levels? - but wherever we

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have had to make assumptions of our own, rather than drawing on the published work of specialists in the field, we have tried always to be conservative. What is disturbing to me is that I know of no other published attempt to determine the order of magnitude of the risk. I recognise the immense difficulty of being able to speak with certainty when results have to be extrapolated over at least six orders of magnitude. But where the need is great, some effort should be made: in its absence the discussion is left wide open for pure speculation undisciplined by any facts.

So far I have discussed two problems which require us to apply much more thought to the relationship between Maltoni's animal results and the known human data. A third problem exists which is, for industry, much more important than the previous two and which concentrates our attention exclusively on better analysis of human information.

Throughout the past 2½ years one group of people has shown a maturity and a sense of responsibility and of determination which is an example to the rest of us. This is the industrial workforce actually engaged on producing PVC. Clearly all of us - medicals, engineers, chemists, legislators - had to establish conditions which were safe for work, but, with that achieved, our obligation to the work people is not yet fully discharged. We, and they, know that, in the future, there will be further cases of angiosarcoma of the liver among vinyl chloride workers, deriving from the higher exposures of earlier years. When these occur, there will be an inevitable diminution in their sense of security; and doubts will naturally arise, for them and their wives and families, about the effectiveness of the new safety measures. If this happens, we who helped to devise the regulations will not have done our duty if we can only reproduce the same qualitative reassurances that we were using in 1973 and 1974. With the finalising of regulations around the world the job - for doctors, administrators, statisticians and general managers - is not finished. We must be in a position to reassure those most directly concerned that we have done our job well; and this requires us to pursue our research and our analyses further and further towards a quantitative conclusion.

What, you may ask, can be done? I'd like to devote the last section of this paper, to a brief review of what has been done on data analysis and then to suggest a scheme for further work. These latter proposals derive from many discussions I have had with my colleagues Dr Williamson and Dr Paddle of ICI who would be much better equipped to present them today: I must present them in simple layman's terms for that is the only way I know.

Until early 1976, the only formal document which surveyed the world data on the effect of vinyl chloride on humans was the NIOSH list of angiosarcoma cases among vinyl chloride workers. But this was only a list; no analysis of any kind was attempted.

In April 1976, the CEFIC document, to which I have already referred, made a first step in classifying the human data. It listed the cases according to the particular plant on which they occurred; and it summarised its findings in the following (up-dated) table.

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TABLE 1

<u>Number of A/S Deaths/Plant</u>	<u>Number of Plants</u>	<u>Location of Plant</u>
10	1	USA
9	1	Canada
3 each	2	USA
2 each	6	Germany, Sweden, France + E Europe
1 each	13	USA + Europe
<u>50</u>	<u>23</u>	
No cases reported	~20 plants with >20 years life	

Many of us believe that this rather puzzling distribution can only be explained on the basis of differing exposure levels, many years ago, from one plant to another and that this is the first indication that some sort of dose-response relationship might be deduced for man. If it does - and Maltoni has certainly demonstrated one for rats - then we should be doing all we can to determine it. Before considering how this might be done, let us see whether the Crude data can tell us anything else.

If the deaths are tabulated, by year of death (where we know this) we get the following information.

TABLE 2

<u>Years of Deaths</u>	<u>Numbers of Deaths in Period</u>	<u>Average Number of Deaths/Year</u>
Before 1961	0	0
1961-65	2	0.4
1966-70	10	2.0
1971-75	24	4.8
1976 so far	4	>4.0
	<u>40</u>	

At first sight this is alarming since the number of deaths/year appear to be on a rapidly ascending curve; but before we proceed, it is worth looking at another classification, which I have not seen published elsewhere. If we group the deaths according to the year of first exposure, we get results which I have summarised in Table 3.

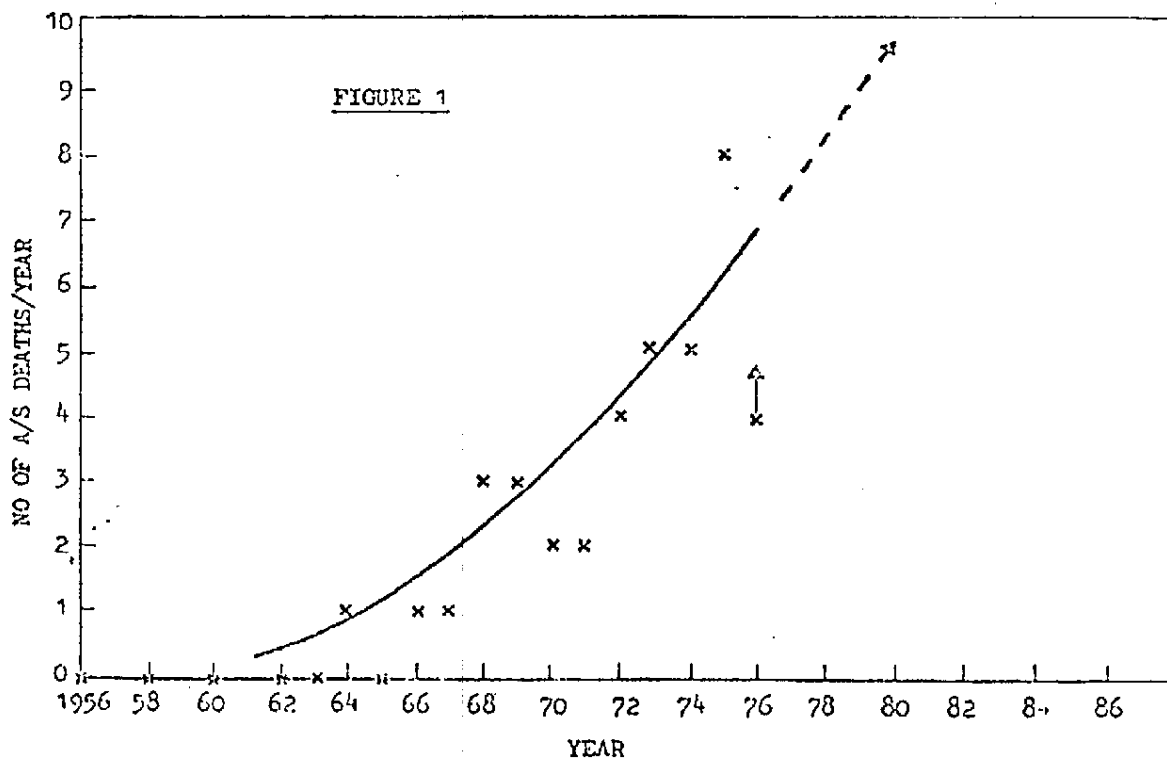
AP00048819

TABLE 3

<u>Years of First Exposure</u>	<u>Number of Cases</u>	<u>Latency Period from First Exposure</u>	
		(a) Range (years)	(b) Number of Cases With <15 Years Latency
1943-54	28	15->32	0
1955-66	14	9-20	8

In the second of the two 12-year periods the fact that we have no latency periods > 20 years is not of course surprising. The elapsed time has not yet been sufficient for longer latencies to appear; and regrettably we must expect further cases to arise. What is interesting, however, is that 8 out of the 14 cases in this period have latencies less than 15 years whereas, in the first period, no latencies as short as this have been reported. It seems difficult to believe they did not exist: indeed this analysis seems to provide the clearest evidence yet in support of the suggestion that, prior to 1961 and possibly later, deaths from angiosarcoma were under-recorded.

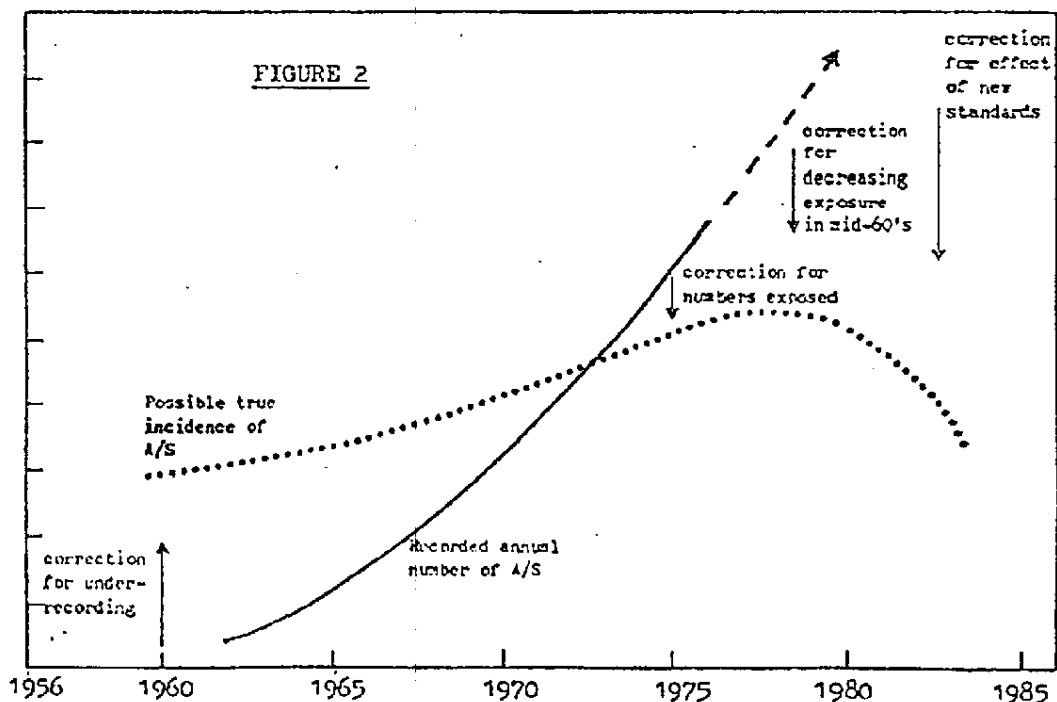
We can best see where this takes us by looking at some simplified graphs. If we plot actual numbers of deaths per year against the year, we get the following picture (Figure 1), which is disturbing if true.



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However, we have seen that early deaths are probably under-recorded, so the real line has, almost certainly, a lower slope than this. Further, the industry, and the numbers of people becoming at risk each year, grew rapidly in the 1950's and 1960's so that if we were to plot the incidence of deaths, i.e. the number of deaths each year as a proportion of the population at risk, say 20 years earlier, then we would expect the righthand side of the graph - and its extrapolation - to decrease relative to the earlier years. A further factor still is that exposure levels have steadily decreased over the past 20-30 years, from values of possibly 1000 ppm in the 40's and 50's to values below 200 ppm in 1973, immediately before the recognition of vinyl chloride as a human carcinogen. Since we believe there is a dose-response relationship, these changes should result in a decreasing incidence by the late 1970's. By 1985, the effect of the latest standards should be quite marked; we must expect, still, some 30 year latencies dating from 1955 (but what about Maltoni's BT3 results?) but there ought to be no 12 year latencies dating from 1973, and I hope there will be few 20 year latencies dating from 1965.

Figure 2 shows the original line of Figure 1 with arrows suggesting likely changes because of the factors listed above. A very notional revision is indicated by the dotted line.



AP00048821

Can we get a better idea of where this new line really is? As an amateur who doesn't therefore see the difficulties may I suggest

- (a) that our statisticians might be able to give some estimate of the number of missing cases in the early years and
- (b) that industry, with some difficulty, ought to be able to estimate the yearly populations at risk.

To estimate the effect of reduced exposures, we need to know what the exposures have been over the whole period and we need to know the dose-response effect for humans. These are much the most difficult problems; but indications of exposures have been given by industry spokesmen and some refinement of these must be possible. With these available, the human mortality data may be susceptible to analysis. In addition, we need a detailed development of a dose-response relationship for rats, from Maltoni's data. At best this relationship may be cohesive with and supportive of any tenuous relation we develop from human information: at worst we may have to use it alone, possibly with arbitrary factors applied, since the crude data does seem to suggest that rats may be more sensitive than man to vinyl chloride.

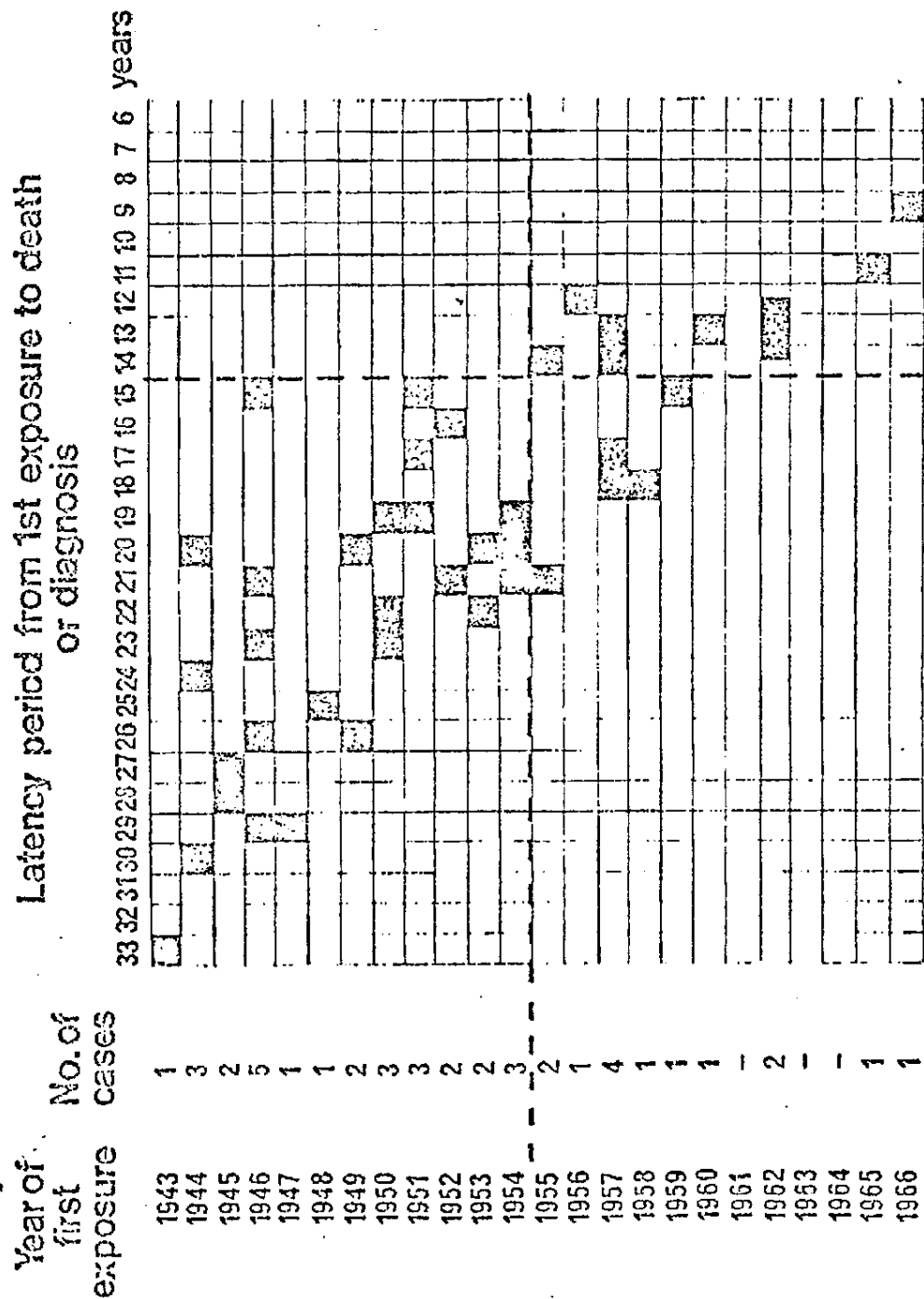
A dose-response relationship is essential for the last correction which requires the calculation of the risk of getting angiosarcoma in 1935 after exposure to only a few ppm of vinyl chloride. This may be difficult, but we have a duty to the people in the industry to attempt it. Perhaps we do not have to be overprecise, for if we are correct in believing our new standards to give a large margin of safety, the calculation of extremely low risk at these exposures may not be too sensitive to errors in the extrapolation.

All this then needs to be done. What is being done? Within ICI, my colleagues Dr Williamson and Dr Paddle are working on the problem, but it is difficult within one company to achieve everything, for the data available to us in ICI may not be representative of the world situation. Nevertheless I believe they will be able to publish some preliminary observations shortly, and I know they would welcome comment, suggestions, or involvement with them, on the subject.

The word "involvement" brings me back to my subject of "interactions". When the task - of devising safe operations - was clear, many institutions in Europe interacted well and achieved much. I've tried to show that much remains to be done: so let interaction, co-operation and contribution flourish still. As another of my colleagues, Dr John Stafford, has put it "the sooner we address and apply ourselves ... unreservedly to ... the task ..., the sooner we shall have really well-founded data to satisfy ourselves, our neighbours, customers, critics etc that the VCM health problem has not only been satisfactorily contained but finally solved."

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AP00048823

indicates no link to PVC, defects

By JIM SPEROS
Telegraph Staff Reporter

A survey by The Telegraph indicates no apparent connection between the occupation of parents of children born in Painesville in 1973 and the abnormally high rate of birth defects in the area for that year.

The Ohio Department of Health reported in August that it was investigating reports that three northeastern Ohio communities, including Painesville, had double the statewide average of birth defects for 1973. The reports linked the defect rate to the use of vinyl chloride in industrial plants in Avon Lake, Ashtabula, and Painesville.

Painesville had 826 births in 1973 with 23 born with birth defects or congenital malformations. This gave the city a rate of 27.8 defects per thousand as compared with a statewide average of 11.2 defects per thousand births. Reports from the AFL-CIO Industrial Union Committee had indicated that the defects in several communities might be related to the use of the chemical, used to make polyvinyl chloride, the most common form of plastic.

The Telegraph survey found that of the 23 children born in 1973 with defects, only one had a parent working at either Uniroyal or Hobasite, the two area plants that use vinyl chloride. In the control group of parents of children born normally that year, one also worked at a vinyl chloride plant prior to his child's birth.

Similarities also existed between groups of parents who worked in chemical plants where vinyl chloride was not used, and also between groups of parents who worked in plants or careers in which volatile chemicals were not used at all.

No correlation could be found between the type of defect in the child, or residence of the parent, and occupation. A cross tabulation of those variables produced only random patterns. Hyaline membrane disease (a disease that prevents air from entering the bloodstream in the lungs) was the most common defect, and Painesville, Madison, and North Madison were the communities with the highest concentration of births in both groups.

625
applied
in polling

The Telegraph survey on possible effects of the use of vinyl chloride in two area plants and the abnormally high rate of birth defects in the area was done using scientific polling techniques.

Each certificate of birth at the Painesville City Health Department is numbered consecutively. The certificates also show whether the baby was born with any kind of birth defect and the name and address of the parents.

Each birth certificate that noted a baby born with a defect was made part of the sample called the "experimental" group. The name and address of the 23 children born with defects in 1973 was taken as the basis for polling.

To select a "control" group, or group that accurately represented the entire population of babies born in Painesville in 1973, a random selection process was used. A number between one and 35 was selected at random, and the certificate with that number made part of the control sample. Each subsequent 35th certificate after that was also made part of the sample to make a control sample of 25, approximately the same number as in the experimental sample. Because the first certificate was chosen at random, each birth had an equal chance of being included in the control sample. In three cases, the 35th subsequent certificate could not be included in the control sample, either because it was one included in the experimental sample, or because the baby was adopted and the identity of its parents could not be determined. In each of the three cases, the next certificate was taken, and the selection of subsequent respondents taken based upon the original number.

selected in both groups by telephone and field work. Respondent that they had been selected to participate in an occupational survey. The respondents were then asked the occupation of both parents, the company they worked for, and the length of time with that company. When either parent had worked for his or her present employer for less than five years, the respondents were asked the name of the former employer and the dates worked in an attempt to determine the employer just prior to the time the baby was born.

If the respondents could not be reached by phone, either because there was no current listing or because there was no answer after repeated attempts, the occupation of the respondent was determined by using various directories for 1972 and 1973. In two cases in the experimental and 12 cases in the control group, the respondents could not be reached and had no listing in the directories, and their names were discarded from the sample.

The answers from the respondents were then placed into four categories.

The first category included those who had worked at either Uniroyal or Hobasite just prior to the birth of their child in 1973.

The second category included those who had worked at either a plant in which PVC or other volatile chemical was used, or worked as a laboratory technician where the worker was in contact with chemicals of various nature throughout the working day.

The third category was used for respondents who worked in plants or jobs that had no connection with the VC or PVC industry or had no contact with chemicals.

The fourth category was used for those who gave the interviewer insufficient information with which to place that respondent in any of the first three categories. The results of the entire study can be found in the tables.

AP00048824

Britain's 'OSHA' has second thoughts about VCM

An article in a recent issue of the British Medical journal suggests that vinyl chloride monomer may not be as serious a hazard as was formerly supposed.

In that publication (Oct. 7, 1977), Dr. Peter Baxter and three other doctors who are affiliated with the Health & Safety Executive (a British government agency similar to our OSHA), reviewed the preliminary report by the agency on the incidence of angiosarcoma (liver cancer) in Great Britain.

Specifically the report looked for any correlation between incidence of the disease among workers and in the general public around factories where PVC resin is manufactured or processed.

Reviewing health records for the 10-yr period of 1963-73, the study states that of the 47 cases of liver cancer reported, in only 14 instances was the diagnosis confirmed. Further, of those 14 cases, only one could be "confidently associated" with exposure to VCM. In that instance, the worker had probably been exposed to VCM concentrations exceeding 200 ppm in air for more than 20 years. The VCM exposure standard in Britain is 10 ppm averaged for an 8-hr day.

Turning to the statistics for the general population, living near PVC-using plants, the study found one confirmed case of angiosarcoma, a man who lived within half a mile of such a plant for 6 years before his death. However, no correlation could be found between the incidence of the disease in the general population and the location of PVC operations.

The report also failed to find any cases of the disease that could be attributed to ingesting VCM from foods contained in PVC packaging materials.

Based on that 10 year period, the article's authors concluded that the incidence of this type of cancer in Great Britain appears to be considerably less than 10 cases annually in a population of 50 million and that only one case of the disease diagnosed during that entire 10-yr period could be definitely associated with VCM exposure. The authors, however, did not dismiss the possibility that angiosarcoma could be caused by low-level exposure to VCM and endorsed a continuing monitoring of the situation.

Commenting on the study, a spokesman for the Employment Medical Advisory Service, the parent

organization of the Health & Safety Executive, stated: "The findings give us grounds for hope that the chemical will turn out to be less of a cancer risk than when the American findings were announced."

U.K. plastics production posted gains in '77

Though final figures for the year are not yet available, plastics production figures for the first 6 months of 1977 indicated that the year may end up about 6% higher than 1976.

Based on the first half of the year, 1977 plastics production totalled 1,356 million metric tons (about 3.56 billion lb). This represents an annual rate of about 2.7 million tons, compared to 2.56 million tons in 1976. Considering the lethargic state of the

	(1000 metric tons)
Alkyds	72.4
Polyesters	34.1
Amines	92.0
Phenolics	29.8
Epoxides	11.2
Polyurethanes	38.4
Other thermosets	166.9
Total	444.8
Acrylics	33.3
Polyethylene	264.5
Polypropylene	133.3
PVC	208.1
Other vinyls	5.7
Polystyrene (crystal)	34.2
Polystyrene (impact)	53.9
Polystyrene (expanded)	29.4
Other styrenes	5.3
ABS	16.6
Polyamides	16.4
Other thermoplastics	14.7
Total	851.6
Total	1296.4

British economy, this performance is viewed as reasonably satisfactory.

Looking at specific resins, there was no major growth area. Both polypropylene and polyethylene ran ahead of '76, though PVC production remained level.

With the exception of polypropylene, there was no major shift in the level of exports or imports. PP, however, was up about 34% on an annualized basis over the 71,000 metric tons shipped in 1976. Imports of PP were up almost as much, about 26%. The accompanying table shows the U.K. production by resin for the first half of 1977.



This 1400 mm (47 in.) polyethylene pipe was recently extruded on a 160 mm (6 1/2 in.) extruder in a trial run at the builder's plant before shipment to a pipe producer in Europe. Designed and built by Luigi Banderi S.p.A., Rusto Arisio, Italy, the extruder has a rated output of about 1550 lb/hr and can produce pipe of up to 55 in. dia.