

Meeting with Professor Maltoni, arranged by Ethyl Corporation, and held at
International Hotel, Kennedy Airport, New York City on June 5, 1974.

Present: Jim Bergan, Product Manager, Ethyl Corporation
Auguste Gosselin, Solvay
Walt Harris, IH and Toxicology, Uniroyal Corporation
Maury Johnson, Medical Director, Goodrich Corporation
Howard Kusnetz, Industrial Hygiene, Shell Corporation
Kenneth S. Lane, Ass't. Medical Director, Union Carbide
Professor Maltoni, U. Bologna
Bill Rinehart, Chairman, IH, Ethyl Corporation
Mayo Smith, Industrial Hygiene, Air Products
Mr. Sobel, Statistician, Ethyl Corporation
Ted Torkelson, Toxicology, Dow Chemical Corporation
Roy Wilkins, Business Manager, Ethyl Corporation
M. R. Zavan, Medical Director, Ethyl Corporation

Dr. Rinehart called the meeting to order, and introduced each of the attendees. Mr. Gosselin began the discussion with a chronological summary of the European experiences along these lines:

Solvay discovered some cases of acroosteolysis in 1963. In 1965, they contacted some of the other European producers and told them of their findings. By 1968, a total of 12 cases were known in Europe. That year, they stopped manual cleaning of autoclaves - no more entry into autoclaves. They have had no further cases. Also in 1968, the producers agreed to fund research, and contacted Dr. Viola to find the answers to three questions:

- 1) Is their predisposition to develop acroosteolysis?
- 2) Is it possible to predict who will develop the condition?

012-1974-00004402



Vinyl Chloride
Digital Process Innovations, Litigation Support
(504) 522-3850

UCC
005768

3) Can it be produced in animals?

An exposure level of 30,000 ppm was selected, and animal exposures begun.

In 1969, Dr. Viola reported lung cancers, and zymbal gland cancers had developed in some of the exposed rats. This was disclosed to the sponsors, and later that year presented at a meeting in the Far East. In 1970, the data was presented at the Houston meeting, and published in the Journal of Cancer Research in 1971.

In November of 1970, the sponsors decided on further research, and in July 1971, the four companies agreed to have studies done under the direction of Professor Maltoni. These were projected to take 2½ to 3 years, were to be confidential until completed, and were then to be published in Florence in the Fall of 1974.

In 1972, Dr. Maltoni found angiosarcoma and nephroblastomas in his animals, and further cases developed in 1973.

In 1972, Dr. Dinman contacted the sponsors at the request of MCA. A secrecy agreement was signed between MCA and the sponsors, which arranged for the exchange of all information about the research and the findings. As a result, in 1973, three U. S. representatives of MCA visited Professor Maltoni, and were given all details of his research. Both the Europeans and the U. S. producers started epidemiological studies in mid-1973.

In June of 1973, the U. S. group requested that they be permitted to disclose all findings to date to U. S. Governmental agencies. (NIOSH). The Europeans agreed, but notified their own governments of their findings first. This consisted of contacting the medical officers in the

012-1974-00004403



areas where the plants were located in France, Italy and Belgium. In Germany, the plant managements were notified, although they had not participated in the study - they responded that they had no problem, and did not notify their local officials.

Until the first human case was ~~formed~~^{FOUND} in ICI, there was no further action in Europe.

The current situation in Europe follows:

United Kingdom - There is the most concern here in all of Europe because of U. S. reports being readily available in common language.

Holland - Most difficult situation in Europe, because they have the strongest labor unions in Europe, and these unions are working for the ban of all PVC.

Belgium - Has a new government which does not have a majority in legislature, so they are mostly occupied with politics. There has been no official response there.

France - No government response as yet.

Italy - The Minister of Work gave the media the results of the studies and the known human cases at a news conference. The Ministry of Health has organized a committee to evaluate the situation, and recommend a course of action. The Province of Tuscany has decided to do an epidemiological study of a Solvay VCM factory town, to include both workers and residents. (Dr. Viola is the factory doctor.) A Solvay survey, ^{IN THIS DATA} has ^{PLA} found no cases. Dr. Maltoni says death certificates are not especially reliable in Italy. He feels that without autopsy reports, most cases will be missed. He says Tuscany is not an area with a high incidence of cirrhosis.

6/5/74.5 VCT2 UCC 5768 -5777

012-1974-00004404



Page Number 003 Europe 1

Baggett, McCall & Burgess

UCC
005770

-4-
(DYNAMIT NOBEL)

Germany - There is one plant employing 120 people that has had 70 - 80 cases of acroosteolysis - they also have a high percentage of liver and spleen abnormalities. They have published 2 or 3 papers about their findings - Dr. Maltoni thinks they are optimistic in their conclusions.

Sweden - Two human cases of angiosarcoma reported. Government has established 20 ppm TWA and 50 ppm MAC. Unions are asking that these limits be decreased.

CEPIC - Cooperative European Federation of Industrial Chemical (Producers or Manufacturers) - the various VC producers have agreed to cooperate through this organization, and a sub-committee composed of one representative from each country in the EEC has been formed. All are from industry except the German member. This sub-committee has had one meeting to date with EEC officials in Brussels.

Dr. Maltoni reports the fibrosis of the liver found is a characteristic one - it is more cellular than the fibrosis caused by other agents. He plans a meeting for this November for a group of pathologists, to discuss the characteristics of the tumors (nephroblastomas, angiosarcomas, neuroblastomas, etc.) found in the experimental animals, and the criteria for diagnosis. They want to try to determine precursors and progression. He does not know if there is a relationship between fibrosis and angiosarcoma - they are starting research to delineate this if possible.

Johnson - Incidence of observed/expected cancers per TCA in ~~Lowse~~ ^{Lowse} ville plant:

before 1965 - 0.8

1965 - 70 - 1.5

after 1970 - 2.1

These malignancies included 4 in the brain, 2 glioblastomas, and 2 astrocytomas.

Smith - TCA study reported cancer of the brain. O/E 2.1% vs. 0.4% in their epidemiological survey - 7 cases total.

Zavon - Referred to Mancuso's 1962 study reporting an increased incidence of cancer of the central nervous system in Akron, as compared to Ohio. This study was one using death certificates. Mancuso attributed the increase to the rubber industry because of their predominance in the local industries. Dr. Maltoni said he had paid particular attention to bibliographies of papers appearing since then, and had found no references to this paper - he had concluded the study had ^{been} judged to be of little significance, and thus not cited. My impression is that Dr. Maltoni doesn't think much of Dr. Mancuso.

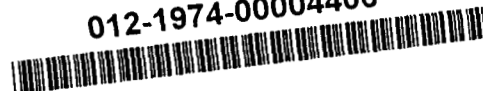
Torkelson - Dow's internal epidemiological survey shows an increased incidence of tumors of all kinds where exposures to VCM has been over 200 ppm. - at less than 200 ppm they found a normal incidence.

Johnson - Harvard University reports increased cancer incidence in Louisville plant (including angiosarcoma). Goodrich is going to ask them how it looks if angiosarcoma are subtracted.

Maltoni - All Italian plants are being asked to do epidemiological studies by the authorities. They propose screening all workers - history and physical, X-ray hands, vascular fragility, complete blood count, sputum and urine cytology.

1970 - Montessori VCM workers showed changes in sputum cytology.*

012-1974-00004406



Vinyl Chloride
Digital Process Instruments, Litigation Support
(504) 522-1850

UCC
005772

His hospital does 80,000 cytological exams per year. He doesn't believe nephroblastoma will shed cells in urine.

*Sputum changes were "unusual changes, not neoplastic or preneoplastic, but were unique."

Gosselin - (Europe) 1945-55 estimated exposures to VCM were more than 1,000 ppm. In this period, the only concern was risk of explosion.

1955-60 Process was improved, and estimated exposures were 400-500 ppm.

1960-70 Exposures were reduced to about 200 ppm, prompted by discovery of AOL.

Mid-1973 Estimated exposure level was 150 ppm.

Now - Estimated exposure level is 50 ppm.

Industry estimates it can get to 25 ppm in 1 to 2 years, and can get to 10 ppm in 5 to 10 years.

Torkelson - Dow plans to get some data on skin absorption for the June 25 meeting. He doesn't know yet if this will be human or animal data.

Dow and Ethyl are both getting data on the efficiency of charcoal filters.

Ethyl is using airline respirators - the emergency standard says only self-contained respirators are to be used.

No one knew what materials are impervious to VCM.

Total vinyl industry estimated to be \$33 to 50 billion/year.

The University of N. Carolina is surveying mortality and morbidity in union (URW) plants of Uniroyal and several other rubber company plants.

Harvard is doing similar study for Goodrich and Armstrong.



be carcinogenic.

In response to the question, "What animal work should MCA sponsor?", Dr. Maltoni said he thought similar inhalation studies, but using a different strain of rats, and using guinea pigs - he didn't see any gain from using mice or hamsters.

His group is now doing high intermittent exposures.

He doesn't feel that using larger groups of mice as proposed by MCA will be very informative.

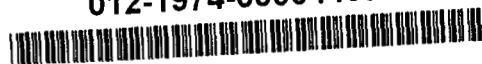
In July of 1973, a European scientist came to the U. S. to visit a government lab (Agency was in NIH), and asked them if they were familiar with Dr. Maltoni's work. He was told that all of the information was available to them, and was shown graphs and tables giving detailed results. The Agency was said to be planning a large research project on VC - it was not NIOSH. Dr. Maltoni says it should have been impossible for them to legitimately have this information at that time, and he was unhappy about it.

Wilkins says that a manufacturer of asbestos pipe and vinyl pipe were told by a government agency that the vinyl problem existed, about the middle of 1973. There are only four such companies - Johns Manville, Capco, Certainteed and Flintkote.

The Europeans are also undertaking the following types of metabolic studies in rats:

1. Devise a method of analysis for VC in biological fluids.
2. Study the distribution in the body systems and excretion through different routes at varying dose levels.
3. Identify metabolites.

012-1974-00004409



Vinyl Chloride
Digital Process Innovations, Litigation Support
(504) 522-7850

UCC
005775

4. Relationship of metabolites to oncological and pathological effects.

They are also initiating studies in rats and monkeys on chronic toxicity of VC, other than tumors:

1. Behavior, histological, hematological and biochemical.
2. Effect on liver function in mouse, rat, GP and dog.
3. Effect on synthesis of macromolecules.
4. Effect on blood coagulation and vascular function.
5. Effect on liquid metabolism in rats and rabbits.
6. Effect on endocrine system.
7. Effect on reproduction through 3 generations.
8. Effect on immune systems.

They expect these projects to take 2 years.

The Europeans expect to have a delegation at the OSHA hearings, but do not know if they will make a presentation.

Dr. Maltone refuses to estimate a TLV. In answer to my question about liver function studies, he says it is a waste of time and money as a screening method in VC workers.

In the discussion by the group, it was stipulated that the only arguments possible at the hearing are that 25 to 50 ppm are so drastically low compared with earlier exposures, that the existing numbers of angiosarcomas will become non-existent. Or, using animal data, 50 ppm means that the animal lives out a normal life span, and cutting this even lower would mean the incidence would decline to non-detectable limits.

No one has obtained a copy of the 1949 Russian paper on the effects of VC, mentioned by Selikoff at the Academy of Science Meeting.

6/5/74.5 VCT2 UCC 5768-5777

012-1974-00004410



Page Number 009 Europe 1

Baggett, McCall & Burgess

UCC
005776

Dr. Maltoni says rats will develop CA lung with more than 100 agents, but the mouse will not develop it with anything he knew about. They were unable to produce ^{PRIMARY} CA of the lung in their mice by inhalation, although they did find metastatic lesions *IN THE LUNG.*

Goodrich says they are now at 20-25 ppm - Uniroyal says they are not down that low yet.

Harris said that the University of N. Carolina did an epidemiology study in the rubber plants in N. Carolina, and did not confirm Mancuso's study re CNS cancer. This study has not been published.

Smith said he had spent two weeks in Sweden, and had information on their exposure levels to VC, which he was not at liberty to disclose. He says they were "high".

Tork's comment is that things can only get worse - that an attempt will be made in all future angiosarcomas to causally relate them to VC. And the animal data being positive will only increase the adverse publicity about the industry.

On this happy note the meeting closed.

K.S. Lane MD

012-1974-00004411



UCC
005777