

UNIROYAL, Inc.

Oxford E-G-1

(Location)

TO: C. D. McCleary ✓
R. E. Lowell ✓
D. E. Dudrow ✓

FROM: W. D. Harris
Industrial Toxicologist

DATE: October 30, 1972

SUBJECT: Vinyl Chloride

The attached letter was sent handwritten to Dr. George Best of MCA from Europe on hotel stationery because of short time before our already planned November 14 meeting in Washington.

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INTERCOMPANY CORRESPONDENCE



UNIROYAL, Inc.

Oxford Management & Research Center
Middlebury, Connecticut 06749

October 20, 1972

Dr. George E. Best
Manufacturing Chemist Association
1825 Connecticut Avenue, N. W.
Washington, D. C. 20009

Dear Dr. Best:

Please excuse this handwritten report. I felt it best to get it to you as quickly as possible. We met yesterday at 4:00 p.m. in the office of the Medical Director of Montedison in Milan about one hour later than scheduled due to their breaking up late for lunch.

The work is being done here in Bologna by Professor Cesare Maltoni, Istituto di Oncologia, Viale Ercolani 4/2, 40010 Bologna, Italy. At the request of the European committee, I went to Bologna accompanied by Professor Maltoni and D. P. Duffield, M.D., Medical Director of ICI's Mond Division. Professor Maltoni was most gracious and showed me where they are doing their work in an old castle outside Bologna, their treatment chambers, analytical procedures and how they keep their records. We went back to the hospital where I saw their histopathological set-up.

Without going into detail at this time, I will summarize by saying that I see no point in carrying out the study which we had originally planned. Professor Maltoni is in charge of the cancer treatment and research at the University Hospital which serves the whole province around Bologna. Consequently, he is in a perfect position to know completely the problems of human cancer. He is not an alarmist. He feels VC can be used safely but that the caution flags are up and we will need good data.

Professor Maltoni knows Dr. Viola and says that his pride was hurt badly by the treatment he received at Houston and at Ostend. His work had many weaknesses and he apparently was worked over pretty well by some of his colleagues. He is continuing his studies at high dosages. He is organizing and heading a worldwide conference to be held in Italy in October 1974. Professor Maltoni expects that he will make a strong bid to vindicate himself at this meeting. Since Professor Maltoni's own work has given "surprising" results at the highest levels, he feels that it is imperative that the industry present the best possible countering data in order to show that VC can be used safely. He feels that certain additional work is indicated. The European group feels so strongly about this that they

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October 30, 1972

REPORT OF MEETING WITH EUROPEAN GROUP ON VINYL CHLORIDE MONOMER STUDIES

We met at the office of Professor Dott, Emilio Bartalini, Medical Director of Montedison, on October 19. His office is about 3 or 4 blocks from the main office of Montedison in Milan. It was obvious that they had fairly extensive medical facilities somewhat comparable to that of a large American chemical company.

Those present were

For Imperial Chemical Industries

Mr. D. M. Elliott

General Manager-Production

Solvents and Monomers Group

Mond Division

The Heath, Runcorn, Cheshire

England

Telephone: Runcorn 3456

Telex: ICI MONDHQ RUNCN 62655

D. P. Duffield, M.D.

Division Medical Officer

Mond Division

Castner Kellner Works

Runcorn, Cheshire, England

For Solvay et C^{ie}

Dr. Marc Y. Lefevre

Medecin Toxicologue

Direction Centrale du Personnel

33 rue Prince Albert

1050 Bruxelles, Belgium

A. Gosselin

Dirigeant Produits Vinyliques

For La Cellophane

A. Valland

Ingenieur (sp?) Council

18 Place Henri Bergson

Paris 8, France

For Rhone-Progil

Dr. Jean Berrod

Medecin (sp?) Chef de le Societe Rhone Progil

47 Rue de Villiers

Neuilly 92, France

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For Montedison

Professor Dott. Emilio Bartalini
Medicina e Igiene del Lavoro
Via Appiani 12,
Milano, Italy Telephone 653026

Dr. Tiziano Garlanda
Protezione Ambientale e Sicurezza
Via Turati 7
20121 Milano, Italy Telephone: (02) 6333 Telex 31679
Montedis
Telephone: Direct dialing 62704085

Professor Cesare Maltoni
Istituto Di Oncologia
Viale Ercolani 4/2
40138 Bologna, Italy
Telephone Area 051 390417 or 393824

W. D. Harris
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Middlebury, Connecticut 06770

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At the outset Mr. Elliott, who acted as the spokesman and interpreter explained that Dr. Maltoni's work which is now past 72 weeks has shown "surprising" results and that certain follow-up work is clearly indicated. He explained that it was the feeling of their group that the interests of both groups would be best served by their inviting our Technical Coordinating Task Group to hold its next meeting in Milan instead of in Washington. They would disclose what they are doing and let me see all technical facilities but would withhold detailed results until the committee as a whole met. They promised that they would disclose all results at that meeting.

Dr. Maltoni explained that there will be a meeting held in Italy in October 1974 under the chairmanship of Dr. Viola. This will draw together cancer researchers from all over the world. At this meeting Dr. Viola is expected to present damaging data on further more careful studies at high levels. Therefore, he feels it imperative that we have the most complete data possible at reasonable levels to show that vinyl chloride can be used safely. The group feels that it would be a waste to carry out our studies as originally planned and that both our interests would be best served by carrying out the rest of the work under Professor Maltoni.

They then proposed that I go to Bologna with Dr. Duffield and Professor Maltoni that night to see first hand his facilities. So I went back to my hotel and gently advised my wife to pick up our things so we could check out and catch the 7:45 p.m. train for Bologna. Professor Maltoni cooperating with Montedison's traffic department had secured a room in a hotel some little distance from the railroad station. Professor Maltoni, Dr. Duffield and I had a lively conversation during this trip of over two hours. After our arrival he took us all out to dinner at a restaurant built early in the present millenium. One little incident gave insight into his basic honesty. While waiting for the taxi he patiently waited his turn in line. When some people started trying to get a taxi out of turn he immediately took over and told the driver who was next. No one argued, though he is not a large man.

In the morning he personally drove Dr. Duffield and me in his own Fiat 124S, an economy family car, out to see the animal work. He had given a great deal of thought to a location which presented a minimum hazard due to explosion and one which would be free of air pollution, excessive noise, etc. He personally designed cages and all equipment and had it built to be free of any contaminants which might complicate the study. Equipment was simple and functional but I felt well designed and very clean. The animal studies are carried out in a separate small building located in a courtyard enclosed by a stone wall at the Castle of Bentevoglia, a 600 year old castle on a 4500 acre estate owned by the University of Bologna.

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It is located in the middle of a farming area.

Maltoni showed me anything I wanted to see and answered any questions on protocol and methods. This is summarized in outline form below:

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.

Records: Very complete, neat and accessible.

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C O N F I D E N T I A L

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.

Control. Vinyl acetate + control 2500 ppm.
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.

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European Project Sponsors:

Imperial Chemical Industries
Solvay et Cie
La Cellophane
Montedison
Rhone-Progil

Research Investigator in charge:

Professor Cesare Maltoni
Istituto Di Ancoologia
Bologna, Italy

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