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Imperial
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Plastics
Division

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FEB 10 1981
BARR

Dr J T Barr
Air Products & Chemicals Inc
Box 538
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USA

Your ref.	Our ref.	Tel ext	Date
	JS/SEW/DSO-16	3162	28 January 1981

Dear John

VCM - MALTONI

You may care to have a copy of a letter dated 22 January which I have had from Dr Tassignon of Solvay. I think this should be helpful to you in your analysis of Maltoni's work. I am inclined to agree with Dr Tassignon that Maltoni's method of handling control animals is important but it will not have much impact on outside audiences.

I was interested that Geoff Paddle had sent to you on a personal basis a translation we made of a very good treatise by Dr Tassignon. I have asked Solvay several times that they should publish this, but my requests have been ignored to date. I thought it was a very helpful paper by Tassignon and so far it has been circulated only to the four Maltoni sponsors in Europe.

With best wishes.

Yours sincerely

J Stafford
Division Manager
Health & Environment Protection

SOLVAY & Cie

société anonyme

direction centrale du personnel

Brussels, 22nd January, 1981.

Réf : DCF/JPT:pdr

Dr J. STAFFORD
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*Dr. C. P. P. P.
Dr. W. C. F. A. A.
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Dr. D. W. K. K.*

Dear John,

In Preparing Newsletter Nr 2 to the members of the VCM Medical Committee, I came across one of your letters dated October 16th, 1980, in which you seemed to be puzzled about John BARR's - Air Products - finding that there are discrepancies between the tables in MALTONI's publications relating to the VCM project.

We were all aware of such discrepancies in the statistical group set up by the sponsors. They are to be explained by the fact that MALTONI repeatedly went back to the raw data and reexamined his slides as well as the tissue blocks.

I went through 9 presentations of the "final results" of experiment BT 1 on Sprague-Dawley rats with concentrations in the air from 10,000 ppm down to 50 ppm :

A. Environ. Res., 7:387, 1974; B. Med. Lav., 65:421, 1974; C. Medichem 2nd International Symposium, Milano 28-29 Oct. 1974; D. Gli Ospedali della Vita 1:7, 1974; E. Ann. N.Y. Acad. Sci. 246:195, 1975; F. Colloque scientifique à la Fondation Curie, Paris 2 Mar. 1976; G. Ann. N.Y. Acad. Sci., 271:431, 1976; H. INSERM Symposia Series, 52:127, 1976; I. Colloque scientifique à la Fondation Curie, Paris 10 Nov. 1979.

There is a first discrepancy between publications A and B. In publication A, the data for the concentrations at 250 and 50 ppm as well as the control group were only provisional since a few animals were still alive. Nevertheless, MALTONI corrected almost all the figures relevant to the other concentrations in the following articles he published in 1974.



...
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The trend was upward. Except for a typing error relating to the number of hepatomas at 500 ppm in publication F, MALTONI presented always the same figures. There is a second discrepancy between the Paris symposium in 1979 and all his previous publications. The trend is upward again, for nephroblastomas, for hepatomas and a substantial rise appeared in the total number of tumour - bearing animals at all dose levels. This is due to the fact that MALTONI went back again to the raw data and picked up new tumours. Other discrepancies in the 1979 presentation in Paris are due to the fact that the number of animals considered to be exposed in experiment BT 1 was reduced to 30 rats per sex and dose. About 5 animals per sex and dose had been added to the study groups during the course of experiment BT 1 for unknown reasons. We advised MALTONI to discard them, view the fact that statistical analysis can only be performed on the homogeneous groups originally planned.

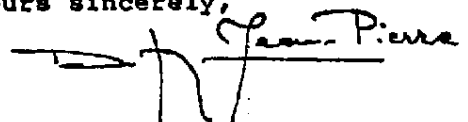
It is obvious, for those reasons, that the data published as the result of the Paris Symposium in 1979 ought to be considered as the reference data.

Another cause of trouble is the fact that MALTONI has a different concept about control groups. During a visit at his institute last month, I learned from the technical manager, DAL ZOTTO, that control animals are never introduced into the inhalation chambers. The occurrence of mammary tumours in the exposed group in many of his studies may be explained on the ground of an enormous difference in stress conditions between exposed and non-exposed animals. Indeed, during an important part of the day the exposed animals are living in stainless steel rather dark chambers (noise), in the draft of the ventilation system and the rotating fans, with no food nor water (in the more recent experiments) and with no contact with the outside world. The animals are packed together and temperature and humidity of the cages rise quickly. In the meantime, the control animals are never removed from normal housing conditions.

This information will not have a great impact however on the case of vinyl chloride but it is an important consideration in evaluating some borderline effects observed by MALTONI in the mammary gland of rats exposed to other monomers. This information is going to be published in the proceedings of MALTONI's presentation of long-term bioassay on ethylene dichloride at the Environmental Health Risk Assessment Seminar on ethylene dichloride in Cold Spring Harbour Laboratory on November 15-16, 1979. As there has been very little reaction in the audience to this information, I guess it will not affect MALTONI's earlier work.

With best wishes.

Yours sincerely,

A handwritten signature in dark ink, appearing to read "Jean-Pierre". The signature is stylized with a large, sweeping initial "J" and "P".

Dr J-P. TASSIGNON.

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NOV 17 1980
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Tel ext
3162

Date
11 November 1980

Dear John

VCM - MALTONI

I have now heard from Mr J C Thomas that the only results we know published on BT12 and 13 were way back in 1976, as you can see from the attached copy of a letter from JCT. My colleague Geoff Paddle tells me that he and others have noticed the same discrepancies which you mention. We have always presumed that the latest figures are the most accurate ones. I think this is as far as I can go in replying to your letter at this time.

At the end of October I was present at the NYAS Workshop on brain tumours and I must say Maltoni was very fair in everything he said about VCM and brain tumours in animals. The Workshop was not a very great event and VCM was exonerated, though OSHA are still determined that there is an excess of brain tumours in the UCC, Dow and Exxon factories or refineries which they have studied, but they don't know which chemical is causing the brain tumours.

With best wishes.

Yours sincerely

J Stafford
Division Manager
Health & Environment Protection