

Monsanto Company
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December 29, 1983

Dr. Myron S. Weinberg
Weinberg Consulting Group Inc.
2828 Pennsylvania Avenue N.W., Suite 301
Washington, D.C. 20007

Dear Dr. Weinberg:

In response to your request concerning Jack Dean's report that someone is studying latent immune responses in man, I have gathered the following information.

Searching our literature for all articles authored or co-authored by Dean I have found only articles dealing with immune functions in rodents and with proposed testing and screening approaches. Copies of the two most relevant articles are enclosed. Dean has, however, referenced J. G. Bekesi et al as writing on "Lymphocyte function of Michigan dairy farmers exposed to polybrominated biphenyls" (Science 199:1207) and R. E. Faith et al as writing on "Chemical separation of helper cell function and delayed hypersensitivity responses" (Cell Immunology 40:275). Unfortunately, we have neither of these latter articles and have had to order them.

I have also searched on the keyword "immune". The most prolific author on the topic of human immunity seems to be G. Reggiani of F. Hoffmann-La Roche & Co., Ltd. In three of his reviews (enclosed) he mentions immunocapability studies of 45 Seveso children. Other than an increase in the complement hemolytic activity all tests were normal over a period of two years. A listing of the tests performed is included in the enclosed article by F. Pocchiari et al.

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Dr. Myron S. Weinberg

December 29, 1983

Reggiani also mentions a study of three groups of adult male workers in the United Kingdom. He does not elaborate on this study other than to say that "Preliminary results could seem to suggest that the exposed groups are relatively deficient in primary immune capability. These findings had apparently no repercussion on the frequency and course of infectious diseases in these people." One of the groups had been "exposed to toxic levels of TCDD more than ten years previously."

If you require any further information, please do not hesitate to contact us.

Sincerely,

William A. Shirley
William A. Shirley

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Encs.

cc: Dr. A. M. Ford

Dr. W. J. McCarville

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MONSANTO POLYMER PRODUCTS CO.
800 N. Lindbergh Boulevard
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September 20, 1983

CONFIDENTIAL
SUBJECT: TCDD

Dr. Myron Weinberg
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Dear Myron:

I must apologize for being slow in answering your letters these past two weeks. With the setting of the Nitro trial date and the increased activity due to our discussions in Washington, I have found myself looking forward to the weekends as a chance to get caught up. In any event, I will try and answer your questions not necessarily in the order you presented them:

- 1) Taking note of your September 2 letter to Dr. Roush: I think that there is general agreement in the literature that the differences between internal administration of TCDD and dermal administration are in terms of the strength and timing of the effect and not in terms of the effect itself. I discussed this with Bob Greenlee at CIIT last week when Jim Wilson and I visited him and he agreed. I might add that Dr. Greenlee and his group are actively pursuing a number of leads in the area of biochemical response, so I consider him a real find in terms of consulting expertise. We must talk more about our visit to CIIT when you have time, but add that Greenlee believes that once the cytosol receptor complex is formed with TCDD's that a branching occurs with one mechanism leading to enzyme induction and one to other responses including mutagenic behavior.

In the same letter you suggest that antibody formation might be used to determine dioxin exposure. I find two problems with this. First, in order for a low molecular weight material like TCDD to generate an immune response, it must react with a higher molecular weight material, classically protein albumin. This hapten albumin reactant then acts as the antigenic material. TCDD is so unreactive that it is hard to see it acting as a hapten. Dennis Flaherty immunologist at our Environmental Health Lab has indicated that