

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

November 10, 1993

James Collins, Ph.D.
Director of Epidemiology
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167

Dear Dr. Collins:

Thank you for your November 3rd letter and the enclosures including the comments regarding your and Dr Acquavella's interpretation of the epidemiologic data base regarding dioxin. We have reached no conclusions regarding the issue of cancer causality as yet. When we do, it will involve all of the evidence available on possible health effects in humans from exposure to 2,3,7,8-TCDD and its isomers, not just the epidemiologic evidence. This includes animal toxicological data, disposition and pharmacokinetics, mechanisms, dose-response relationships, and any other factors that may be influential.

With respect to your paper and Sinks criticisms of it, several questions have been raised that do not appear to have been adequately answered in your March, 1993 letter to the editor which you enclosed. Sinks reiterates his concerns about your study in his own letter to the editor in the same issue. There are, as we see it, actually 3 issues which we also noted independently of Sinks. That is, on page 8, 2nd column, 3rd paragraph down, you describe in detail a total of 106 (56+50) employees who had evidence of chloracne or a "chloracne-like condition" based upon plant records who you appear to have included in your Table 2 under the column named "no chloracne". It seems to suggest that perhaps these 106 workers should have been included under the column called "chloracne". If there was no other chemical present in the workplace that could cause a chloracne-like condition then why would you consider them as unexposed to dioxin?

Secondly, in the same paragraph you also mention that 214 workers were "considered together as having TCDD exposure from manufacturing processes." These same workers were then included as part of the reference group known as "no chloracne" in Table 2. It has not yet been shown or proven that exposure to dioxin is not

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associated with cancer. Therefore, it seems inappropriate to include them as part of a comparison group for the purpose of evaluating the risk of site-specific cancers that might be related to the exposure. An ideal comparison group is one that has had no exposure to dioxins.

Thirdly, narrowly constricting the definition of your study cohort to include workers who were actually on the payroll during the period from 3/8/49 to 11/22/49 would effectively eliminate all employees who left employment prior to 3/8/49 plus those who started after 11/22/49 who potentially could have been exposed to dioxin either before or after this period. Furthermore, some of those workers who did work within this time frame were employed outside the plant where the accident occurred. Is it conceivable that they received no exposure during the accident if they were outside at the time?

Enclosed you will find copies of the correspondence we have had with Dr. Rappe regarding the Nygren, Rappe et al (1986) paper. Based upon this information it is not at all clear which, if any, of these "cases" and "controls" actually were part of Dr. Hardell's published studies. The only finding that appears certain is that the levels of 2,3,7,8-TCDD in all 31 individuals appears to be low while levels of the higher chlorinated dioxins are many times greater. But it is not even certain that any of the 31 individuals sprayed herbicides as an occupation. In fact, only 12 give an indication that they had done some spraying and several of these had such short durations, it is doubtful that this was a regular job in any case. In my opinion, this data is not relevant to the levels of dioxin to which Hardell's cases and controls were actually exposed. That subject still remains a mystery.

Thank you for the comments regarding chapter 7 that you included with your letter, they will be evaluated and considered for inclusion just as the many other sets of comments we have received. Should you have any additional thoughts on the subject please call me at 202-260-5726.

Respectfully,

David L. Bayliss, Epidemiologist
Office of Health and Environmental
Assessment
Office of Research and Development

Enclosures