

Monsanto

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Dr. Marilyn A. Fingerhut
Chief, Industrywide Studies Branch
NIOSH
Robert A. Taft Laboratories
4676 Columbia Parkway
Cincinnati, Ohio 45226-1998

Dear Dr. Fingerhut:

I am sorry I was unable to provide a more timely response to your correspondence of April 24, 1990, but my travel schedule and an illness of one of our staff prevented it. Monsanto is aware Cate Jenkins, acting in a non-governmental capacity, has forwarded to Dr. Donald Barnes, Staff Director, EPA Science Advisory Board, portions of a plaintiff's appellate brief in a lawsuit involving Monsanto. This lawsuit is now on appeal subsequent to a jury's determination that the plaintiffs were uninjured. The accusations of fraud in this brief pertaining to two Monsanto epidemiology studies are utterly false and without foundation.

The Monsanto epidemiology studies called into question are 1) the Zack and Suskind study published in the Journal of Occupational Medicine in 1980, and 2) the Zack and Gaffey study published in Environmental Science Research, Volume 26, in 1983. The Zack and Suskind study was a cohort mortality study of 122 persons at the Nitro plant developing chloracne from exposure to potentially high levels of dioxin resulting from a runaway reaction of a trichlorophenol (TCP) manufacturing process in 1949. The Zack and Gaffey study was performed at the same plant but studied employees with at least one year occupational exposure to potentially low levels of dioxin from a production process of either TCP or 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) who worked at the plant some time during 1/1/55 to 12/31/77, and included some members of the Zack and Suskind study mentioned previously. The analysis employs a proportionate mortality ratio (PMR) approach and focuses on 58 deaths among exposed persons and 104 deaths of non-exposed persons.

The accusation of fraud in these two epidemiology studies have been raised by a person untrained in and unfamiliar with the science and methods of epidemiology. Further, the accusation is based on information she obtained from an on-going trial from a plaintiff's attorney. It is difficult to respond in a scientific

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manner to the pseudo-scientific arguments made by Cate Jenkins based, in part, on an attorney's arguments during a trial.

The two Monsanto studies called into question have been in the published literature for ten years, have been reviewed numerous times by academics and regulatory agencies such as NIOSH, and yet no charge of serious inaccuracies or fraud has ever been raised until now. If there are serious scientific problems in either of these studies, these issues should have been raised in a scientific forum such as a letter to the editor in the journals where these studies appear either by Jenkins or one of the other numerous persons who have reviewed these studies. No challenge in a scientific forum has ever appeared.

The basis for Jenkins' charges are the inclusion and/or exposure classification of certain persons in the two epidemiology studies. Jenkins' accusations of deliberate study misclassification seem to be based upon two pieces of information, 1) a Monsanto audit of the database from which the two study populations were selected, and 2) reanalysis of the two published study results by a attorney during a trial. I will address each of these points in some detail, and then conclude with any impact these issues may have on the data we have given you for the NIOSH Dioxin Registry.

Firstly, Monsanto has an on-going program to automate historical information for use in future epidemiology studies, health surveillance, or plant health assessments. We have been automating historical data for the Nitro plant for several years. During this time, we have automated literally several million pieces of data. Audits for accuracy of these data have been conducted. Our automated historical data at the Nitro plant is virtually complete after 1954 and is continually becoming more complete for years prior.

In addition, over the years, as we have learned more about our historical manufacturing processes, we have refined our definitions of which jobs and departments have had potential for exposure to dioxin. For instance, when Zack and Gaffey did their study in the early 80's, they considered all persons working in either building 34, or building 41 as having potential for exposure to dioxin. Later reconstruction of the manufacturing processes seemed to indicate only persons in particular departments or jobs in these buildings had potential for significant exposure.

Occasionally, we have discovered through automation of job histories and reconstruction of historical manufacturing

processes an employee or two who has changed exposure classifications. These differences, however, have always been very minor, and have never changed study conclusions. As a person involved in doing large scale studies, I am sure you can understand this.

We have gone to great lengths to document changes. In fact, the results of one of our audits is the basis for part of Cate Jenkins' charge of deliberate misclassification of exposure groups. In 1984, we automated our job histories and discovered a few persons whom we thought were exposed and actually weren't, and a few persons whom we thought weren't exposed but were. We informed you of this change in our letter dated 7/23/85. In 1987, we modified our assessment of jobs which had potential for significant exposure to dioxin based on more information on the manufacturing processes. We informed you of this change in our letter dated 7/17/87. Based on these changes a small percentage of persons changed exposure groups in the Zack and Gaffey study.

In Table 1 we compare the original published conclusions of Zack and Gaffey with our current assessment based the changes noted in our letters to you of 7/23/85 and 7/17/87. Our current assessment indicates twenty-one persons thought to be exposed in Zack and Gaffey study were, in fact, unexposed, while one person thought to be unexposed had potential for exposure. Tables 2 and 3 gives the names and Social Security Numbers of the persons who changed exposure classification. Table 1 indicates the original conclusions of Zack and Gaffey were correct, although the risk estimates, represented by PMR, change slightly.

We have also examined data for persons included in the Zack and Suskind study. We conclude all persons in that study were correctly classified. In table 4, we show the source of ascertainment for each of the 122 persons included in this study.

The second source of alleged deliberate misclassification mentioned by Jenkins is based on the reanalysis of the Zack and Suskind and Zack and Gaffey studies by a plaintiff's attorney. During a trial a plaintiffs' lawyer combined cancer deaths incorrectly from several sources to conclude cancer from exposure to dioxin was two times expected levels. The sources for these cancer deaths were 1) nine cancer deaths among persons exposed to 2,4,5-T or TCP from the Zack and Gaffey study 2) eight cancer deaths not counted in the Zack and Gaffey study among the 122 persons developing chloracne from the 1949 TCP accident in the Zack and Suskind study, and 3) one cancer death reported in our 1984 audit mentioned earlier.

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There are many methodological problems associated with combining study results which you are familiar with, so I will not mention them. However, one major flaw must be pointed out. The plaintiffs' attorney counts the numerators, or the number of cancer deaths from the three sources mentioned above, but counts the denominator from only one source, the Zack and Gaffey study. This approach assures the cancer risk will be overestimated. I should point out the risk estimate for cancer in the Zack and Suskind study is 1.00 (i.e., 9 observed 9.04 expected, calculated by a standardized mortality ratio) and in the Zack and Gaffey study is 0.82 (i.e., 9 observed 10.94 expected, calculated by a PMR). Obviously, any correct combination of these data would result in a risk estimate somewhere between 1.00 and 0.82, not 2.00 as the plaintiffs' attorney contends.

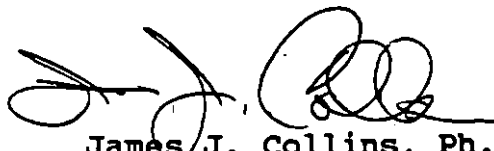
In summary, the accusations of fraud in these two studies are untrue. While there have been some changes in our perception of who had potential for significant exposure in the Zack and Gaffey study, these changes, reported by us, were incorporated to give us a better understanding of the potential for risk from exposure to dioxin. These changes did not alter our original study conclusions. We firmly stand behind the published conclusions of these two studies.

In addition, the erroneous combination of deaths from various sources by a plaintiffs' attorney was not done according to accepted epidemiologic methods and resulted in a major overestimate of risk.

Finally, the updating of the data base which led to a small change in the Zack and Gaffey study results, in no way affects the data we sent you (Monsanto letters dated 11/12/85, 1/21/86, 5/4/87, 1/29/88) for the Dioxin registry. We feel these data are complete and accurate and represent to the best of our knowledge persons who fit your criteria for inclusion in that Registry.

I hope this material and information is useful to your work. Please feel free to contact me if further questions arise.

Respectfully,


James J. Collins, Ph.D.
Epidemiology Director

cc: Dr. Donald Barnes (w/o Tables 2 and 3)

Table 1. Comparison of Zack and Gaffey 1983 Proportional Mortality Ratio (PMR) Study Results with Exposure Determined by Current Work Histories.

Cause of Death	<u>Zack and Gaffey (1983) Results¹</u>				<u>Replication with Exposure Assigned by Work History²</u>			
	<u>Exposed</u>		<u>Unexposed</u>		<u>Exposed</u>		<u>Unexposed</u>	
	<u>Obs.</u>	<u>PMR</u>	<u>Obs.</u>	<u>PMR</u>	<u>Obs.</u>	<u>PMR</u>	<u>Obs.</u>	<u>PMR</u>
All malignant neoplasms	9	82	25	122	6	78	28	121
Buccal cavity and pharynx	0	0	0	0	0	0	0	0
Digestive organs & peritoneum	0	0	3	52	0	0	3	44
Respiratory System	6	168	8	117	5	182	9	123
Genitourinary	2	208	10	370*	0	0	12	349*
Lymphatic and hematopoietic	0	0	1	48	0	0	1	43
Diseases circulatory system	31	117	61	110	20	103	72	104
Diseases respiratory system	2	75	4	62	2	100	4	50
Diseases digestive system	1	27	4	81	1	45	4	72
All external causes	12	129	8	86	7	187	13	139
Total Deaths	58	100	104	100	38	100	124	100

¹ Source: Zack and Gaffey (1983) A mortality study of workers employed at the Monsanto company plant in Nitro, West Virginia. In: Tucker, Young and Grey (eds) Human and environmental risks of chlorinated dioxins and related compounds. Environmental Science Research, Volume 26. Plenum Press, New York, pp 575-591.

² Source: Work history ascertainment and exposure potential based on most recent data.

* $p < 0.05$. Seven deaths from bladder cancer in this category occurred among persons in Monsanto's para-aminobiphenyl registry.

Table 4. Source of Ascertainment for the 122 Persons Included in the Zack and Suskind Study Cohort by Source, Number with Workmen's Compensation Claims, and/or Medical Record.

Source of Ascertainment	Persons Added to Study	Workmen's Compensation¹	Medical Record¹
Letter dated 2/8/49 (H. Boggs to G. Nelson) 2 persons with chloracne developing on or before 2/7/49.	2	2	1
Listing from Safety Office detailing accident of 3/8/49	112	92	53
Memo dated 5/6/49 (E.G. Volz to J.R. Durland) lists 39 cases with 1 additional name.	1	1	1
Memo dated 9/14/49 (E.G. Volz to J.R. Durland) lists 107 cases with 1 additional names.	1	1	0
Memo dated 2/26/51 (E.G. Volz to J.R. Durland) lists 116 cases with 6 additional names.	6	4	3
TOTAL	122	100	58

¹ Some persons have more than one source of supporting documentation for developing chloracne from the accident.