

FAX COVER SHEET

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7 pages (including this cover sheet)

Sent on 22-Nov-93 at 13:14

Comment:

Hi, Paul-- Here is the analysis you
asked me to prepare in Gaffey vs. E.R.F.
I consider this complete and ready to be
reviewed by one or more of our expert
witnesses. I know this is an extremely
busy day for you, so whenever you can
get to it will be fine. Thanks for your
help. --Peter

THE EFFECT OF CORRECTING CLASSIFICATION ERRORS
IN ZACK/GAFFEY'S STUDY OF THE MORTALITY OF DIOXIN-EXPOSED WORKERS

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November 22, 1993

**THE EFFECT OF CORRECTING CLASSIFICATION ERRORS
IN ZACK/GAFFEY'S STUDY OF THE MORTALITY OF DIOXIN-EXPOSED WORKERS**

Background

In March of 1949, an explosion occurred in a trichlorophenol (TCP) process at the Monsanto plant in Nitro, West Virginia, where the herbicide 2,4,5-T was manufactured from 1948 to 1969. As a consequence of the explosion, and of routine operations, many workers and others were exposed to dioxin, an unwanted by-product of 2,4,5-T production.

As a result of dioxin exposure, many workers at the Nitro plant developed chloracne, a disfiguring skin disorder. The deaths of 121 of these chloracne-afflicted workers were studied by Zack/Suskind in a standardized mortality analysis published in 1980.¹ Subsequently, the deaths of routine production workers active for at least a year at the Nitro plant between 1955 and 1977 were studied by Zack/Gaffey who published their findings in 1983.²

Zack/Gaffey concluded that their study did not find "an excess in deaths from any site among malignant neoplasms." [Zack/Gaffey, pg. 590.] In other words, they said they did not find significantly elevated mortality from any cancers among the dioxin-exposed Nitro workers.

After their study was published in 1983, it was reported that Zack/Gaffey had misclassified at least 4 workers.³ Anyone who reads the original Zack/Suskind study and compares it to the Zack/Gaffey study can see that this is true; Zack/Suskind in 1980 listed as "Exposed" 4 workers whom Zack/Gaffey in 1983 listed as

¹ Judith A. Zack and Raymond R. Suskind, "The Mortality Experience of Workers Exposed to Tetrachlorodibenzodioxin in a Trichlorophenol Process Accident," *Journal of Occupational Medicine* Vol. 22 No. 1 (January, 1980), pgs. 11-14.

² Judith A. Zack and William R. Gaffey, "A Mortality Study of Workers Employed at the Monsanto Company Plant in Nitro, West Virginia," in Richard E. Tucker, Alvin L. Young, and Allen P. Gray, editors, *Human and Environmental Health Risks of Chlorinated Dioxins and Related Compounds* (New York: Plenum Press, 1983), pgs. 575-591.

³ Alastair Hay and Ellen Silbergeld, "Assessing the risk of dioxin exposure," *Nature* Vol. 315 (May 9, 1985), pg. 102.

"Not Exposed."⁴

Three of the misclassified workers had died of lung cancer and one had died of Hodgkin's disease, a lymphatic cancer. (See footnote 4 and see Zack/Gaffey's Table 11.)

This paper addresses the question, If the misclassification of these 4 workers were corrected, what effect would that have on the conclusions reported by Zack/Gaffey?

Method

If 4 workers are reclassified to correctly reflect their exposure status (moving them from the "not exposed" column to the "exposed" column in Zack/Gaffey's Table 9) then Zack/Gaffey's Tables 8 and 9 must both be revised.

Table I presents Zack/Gaffey's original Table 8 plus revisions to reflect the reclassification of the 4 exposed workers.

TABLE I
(ZACK/GAFFEY'S TABLE 8 AND REVISIONS)

2-4-5-T Exposure Classification	---Number of Deaths---		----Percent-----	
	Original	Revised	Original	Revised
Exposed.....	58	62	35.6	38.0
Non-exposed	104	100	63.8	61.4
Unknown	1	1	0.6	0.6
Total	163	163	100.0	100.0

Table II reprints the relevant portions of Zack/Gaffey's original Table 9; Table III presents relevant portions of Zack/Gaffey's Table 9 revised to reflect the changes that occur in the data when the 4 misclassification errors are corrected.

When 4 workers are reclassified from the "not exposed" column to the "exposed" column in Zack/Gaffey's original Table 9, it is necessary to recalculate "expected" values and PMRs [proportional

⁴ In Zack/Gaffey's Table 11, these workers appear as (counting from the top), Nos. 5, 6, 9, and 22. In Zack/Suskind's Table 10, these same workers are (counting from the top of the table), Nos. 1, 2, 5, and 7.

The entire Zack/Suskind cohort had chloracne; indeed, the presence of chloracne defined the cohort. Chloracne is a "hallmark" of dioxin exposure (to use Suskind's phrase). [See R. R. Suskind, "Chloracne, 'The Hallmark Of Dioxin Intoxication,'" *Scandinavian Journal of Work, Environment and Health*, Vol. 11, No. 3 (1985), pgs. 165-171.] We therefore know beyond any doubt that Zack/Suskind considered these four workers to have been exposed to dioxin. Therefore, in any subsequent study--and especially in any subsequent study sharing a co-author with the Zack/Suskind study--these four workers should have been classified as "Exposed." In sum, it seems indisputable that Zack/Gaffey misclassified these workers.

mortality ratios]. Since the 4 reclassified workers died of only 2 causes of death (lung cancer and lymphatic cancer), these were the only causes of death that I examined (plus the inclusive categories, "respiratory system" and "all malignant neoplasms" which automatically must change when changes occur in "lung" and "lymphatic").

Using 8 empirically-derived "proportion of deaths" values, which are the same as those used by Zack/Gaffey,⁵ I calculated revised "expected deaths" for all malignant neoplasms, respiratory system, lung cancer and lymphatic cancers, multiplying each "proportion of deaths" by the revised "total deaths" (now 62 among the "exposed" and 100 among the "not exposed"--see Table I, above).

TABLE II
(RELEVANT PORTIONS OF ZACK/GAFFEY'S ORIGINAL TABLE 9)

-----2,4,5-T Category -----						
-----Exposed-----				-----Not Exposed -----		
	Observed	Expected	PMR	Observed	Expected	PMR
All neoplasms	9	10.94	82	25	20.43	122
Respiratory						
system.....	6	3.78	158	8	6.81	117
Lung.....	6	3.57	168	8	6.42	125
Lymphatic...	0	1.35	0	1	2.07	48

Data are reproduced from Zack/Gaffey study's Table 9. See Table III (which presents Zack/Gaffey's Revised Table 9), below.

⁵ Zack/Gaffey calculated an "expected value" for each cause of death by multiplying the total number of deaths (58 in the "Exposed" group and 104 in the "Not Exposed" group) by the proportion of deaths that occurred among "the United States white male population for the time period of study" for each cause of death [Zack/Gaffey pg. 579]. In order to avoid introducing errors into my calculations, I relied on Zack/Gaffey's data for proportions of deaths occurring among U.S. white males for each cause of death. Since Zack/Gaffey did not present the proportions that they used in Table 9, I calculated the proportions from other data in their Table 9; specifically, I divided the "expected" values as given by Zack/Gaffey by the "total deaths" (58 among the "exposed" and 104 among the "not exposed") as given by Zack/Gaffey, thus empirically deriving the proportions that Zack/Gaffey used.

An example, using lung cancer among the exposed population, may help readers understand what I did. I calculated the "proportion of deaths" from lung cancer that Zack/Gaffey implicitly used, among the "exposed" workers, by dividing Zack/Gaffey's 3.57 expected deaths from lung cancer by Zack/Gaffey's 58 total deaths. This showed that Zack/Gaffey used $3.57/58 = 0.062$ as the proportion of deaths occurring among the U.S. white male population for lung cancer in the "exposed" group. In this way, I derived an empirical "proportion of deaths" for total malignant neoplasms, respiratory system, lung cancer and lymphatic cancer among both the "exposed" group and the "not exposed" group, a total of 8 different proportions.

TABLE III
(RELEVANT PORTIONS OF ZACK/GAFFEY'S TABLE 9, REVISED)

-----2,4,5-T Category -----						
-----Exposed-----				-----Not Exposed -----		
	Observed	Expected	PMR	Observed	Expected	PMR
All neoplasms	13	11.69	111	21	19.64	106
Respiratory system.....	9	4.04	222*	5	6.55	76
Lung.....	9	3.82	235*	5	6.17	80
Lymphatic...	1	1.44	69	0	1.99	0

*p < 0.05

Data are from Zack/Gaffey's original Table 9 (which see in Table II, above), except that 3 workers who died of lung cancer and one worker who died of lymphatic cancer [Hodgkin's disease] have been moved from the "not exposed" column into the "exposed" column, and the "expected" values and PMRs have then been recalculated, as described in the text.

After the revised "expected deaths" had been calculated, revised PMRs were calculated by the standard formula, (observed/expected) x 100.⁶

I then calculated 95% confidence intervals for the revised PMRs using tabled values from Breslow and Day for a Poisson-distributed variable.⁷

Discussion

As Table III shows, correcting Zack/Gaffey's misclassification of 4 workers reveals significantly increased (p < 0.05) cancers of the lung and of the respiratory system among dioxin-exposed Nitro production workers.

⁶ As one would anticipate, and as Table III shows, the reclassification of 4 workers from the "not exposed" column to the "exposed" column elevates all four PMRs among the "exposed" workers. The PMR for "exposed - all malignant neoplasms" increases from 81 to 111; the PMR for "exposed - respiratory system" increases from 158 to 222; the PMR for "exposed - lung cancer" increases from 168 to 235; the PMR for "exposed - lymphatic" increases from 0 to 69.

Likewise, the 4 PMRs for "not exposed" workers decrease as follows: for "not exposed - all malignant neoplasms," the PMR decreases from 122 to 106; for "not exposed - respiratory system," the PMR decreases from 117 to 76; "not exposed - lung," the PMR decreases from 124 to 80; for "not exposed - lymphatic" the PMR decreases from 48 to 0.

⁷ N. E. Breslow and N. Day, Table 2.10, in *Statistical Methods in Cancer Research: Volume II - The Design and Analysis of Cohort Studies* [IARC Scientific Publication No. 82] (Lyon, France: International Agency for Research on Cancer, 1987), pg. 70.

This finding reverses the conclusion of the original Zack/Gaffey study.

Thus we can see that significant increases in cancer among Nitro production workers were hidden by Zack/Gaffey's misclassification of 4 workers. As I said in *Rachel's Hazardous Waste News* #171 (March 7, 1990), "In fact, excess cancers have occurred, but it appears that the data have been manipulated to hide the facts." QED.