A Retrospective Job Exposure Matrix for Estimating Exposure to 2,3,7,8-Tetrachlorodibenzo-p-dioxin

Laurie Piacitelli, MS,* David Marlow, BS, Marilyn Fingerhut, PhD, Kyle Steenland, PhD, and Marie H. Sweeney, PhD

Background *A job exposure matrix was developed to estimate the 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure of 3,538 workers who produced 2,4,5-trichlorophenol and its derivatives.*

Methods *Daily TCDD exposure scores that were plant, process, and period specific were estimated for each job title as the product of 1) the concentration of TCDD (μg/g); 2) a qualitative factor to account for the extent of worker contact and 3) time exposed to TCDD contamination. Daily scores were summed to compute individual cumulative TCDD exposure scores.*

Results *Daily TCDD exposure scores ranged from 0.001 to 1,250. Cumulative TCDD scores ranged from 0.002 to 1,559,430. The 393 workers with records of chloracne in the TCDD exposure cohort (11%) had markedly higher cumulative scores than those with no record of chloracne (a median score of 11,546 vs. 77).*

Conclusion *The cumulative TCDD exposure scores incorporate both duration and level of exposure, and permit the relative ranking of worker exposures for the evaluation of exposure–response relationships between TCDD exposure and mortality in an updated cohort study analysis.* Am. J. Ind. Med. 38:28–39, 2000.
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KEY WORDS: dioxin; TCDD; exposure assessment; Agent Orange; 2,4,5-trichlorophenol; phenoxy herbicides

INTRODUCTION

In 1991, the National Institute for Occupational Safety and Health (NIOSH) published a cohort mortality study of workers with exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) [Fingerhut et al., 1991]. Duration of exposure to TCDD contaminated products was used as a surrogate of cumulative TCDD exposure in some analyses. For a subset of 253 workers from two plants, duration of exposure was correlated with serum dioxin levels ($r = 0.72$, $P < 0.0001$). However, the use of duration as a surrogate for cumulative exposure assumes no systematic variation in the average level of exposure over time and among workers, jobs, and plants. Based on a review by NIOSH staff of the operations at these plants, there were inter- and intra-plant, job and calendar time dependent differences in the level of TCDD exposure. Consequently, the use of duration of assignment to processes with TCDD contamination as an exposure surrogate may have contributed to misclassification of the relative exposure levels of cohort members. To reduce this misclassification a job exposure matrix was developed to estimate historic TCDD exposures for exposure–response analyses in a follow-up mortality study [Steenland et al., 1999].

National Institute for Occupational Safety and Health, Cincinnati, Ohio
*Correspondence to: Laurie Piacitelli, NIOSH, 4676 Columbia Parkway, MS R14, Cincinnati, OH 45226. E-mail: lap1 @cdc.gov

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BACKGROUND

Workers were exposed to TCDD during the production of 2,4,5-trichlorophenol (TCP) or one of its derivatives such as 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) ester which was used to formulate the herbicide Agent Orange. Other derivatives included the herbicides 2-(2,4,5-trichlorophenoxy)propionic acid (silvex), 2-(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate (erbon), the insecticide 0,0-dimethyl 0-(2,4,5-trichlorophenyl)phosphorothioate (ronnel) and the bactericide 2,2′methylene-bis-[3,4,6-trichlorophenol] hexachlorophene. The unintentional formation of TCDD occurred primarily during the production of TCP (or its sodium salt) by the hydrolysis of 1,2,4,5-tetrachlorobenzene. The concentration of TCDD in TCP and derivatives depended on process operating parameters, such as temperature, pressure and reaction time, and the level of purification.

The manufacture of TCP began as early as the 1940s, with maximal production occurring in the 1960s due to the demand for Agent Orange in the Vietnam war [IARC, 1997]. Following the war, production was phased out; most uses of 2,4,5-T and silvex were suspended in 1979 and were banned in the United States in 1983 [Fed Regist 1979a, b; Fed Regist, 1983].

MATERIALS AND METHODS

Definition of the Exposure Matrix Cohort

NIOSH industrial hygienists, who were blind to the vital status of workers, reviewed thousands of pages of documents describing processes, job duties and exposures and interviewed long-term employees. Site reports were prepared for each plant and were reviewed for accuracy by the company, and by the unions where applicable [Fingerhut et al., 1984; Marlow et al., 1984, 1986, 1987, 1989, 1990, 1991a, 1991b, 1991c, 1991d, 1997; Piacitelli et al., 1990].

Of the 12 plants in the NIOSH TCDD mortality study [Fingerhut et al., 1991], four were excluded from the TCDD exposure matrix. Plants 2, 5, 6 and 12 were excluded because of limited records describing the level of TCDD contamination in process streams and/or lack of sufficiently detailed work history records. Additional workers from the remaining eight plants were excluded because they lacked adequate records to characterize duration of exposure ($n = 238$) or they worked in a process in which TCDD contamination could not be estimated ($n = 38$). Finally, 727 workers who had exposure to both pentachlorophenol (PCP) and TCDD were excluded to avoid possible confounding in the epidemiologic study by the higher chlorinated dioxins and furans formed as byproducts during the production of PCP. These dioxins are thought to act similarly to TCDD, although they are considered less toxic [IARC, 1997]. Cumulative TCDD exposure scores were estimated for 3,538 workers from eight plants (69% of the original mortality cohort). Table I lists the TCDD contaminated production processes and dates of their operation at the eight plants [Marlow et al., 1984, 1986, 1989, 1990, 1991c, 1991d, 1997; Piacitelli et al., 1990].

Routes of Exposure to TCDD

Dermal, gastrointestinal and transpulmonary absorptions represent potential routes for exposure to TCDD [IARC, 1997]. Dermal contact with TCDD was the most likely route of exposure given the low vapor pressure of TCDD (7.4×10^{-10} mm Hg at 25°C) and its persistence in the environment. Opportunities for exposure due to inhalation to TCDD in the gaseous form were limited; there was the potential for exposure to airborne TCDD contaminated particulates for processes with drying, grinding, and packaging operations. As with other occupational exposures where skin contact has occurred, workers had the potential for ingestion of TCDD due to the transfer of materials from the hand and face to the mouth during activities such as eating and smoking [Roels et al., 1982; Ulenbelt et al.,1990; Far et al., 1993; Karita et al., 1997].

Algorithm for Estimating TCDD Exposure Scores

An algorithm was used to estimate daily TCDD exposure scores that was based on 1) the concentration of TCDD in micrograms per gram (μg/g) in process materials, 2) a qualitative contact factor (0.01–1.5) to account for the extent of dermal contact with TCDD and exposure to airborne TCDD particulates, and 3) time exposed to TCDD contamination, expressed as a fraction of a work day. These three factors were multiplied together to yield a daily TCDD exposure score:

$$\begin{aligned}&\text{Daily TCDD Exposure Score}\\&\quad = \text{TCDD Concentration } (\mu g/g)\\&\quad \times \text{Contact Level } (0.01 - 1.5)\\&\quad \times \text{Time Exposed (fraction of a day)}\end{aligned}$$

The algorithm computes numeric exposure scores which cannot be directly interpreted as dose. It was not known what fraction of TCDD was transferred to the skin from contact with process materials and surface contamination nor what fraction was absorbed via dermal penetration, ingestion or inhalation. Rather, the scores are computed in a consistent manner, to provide a numeric value that can be used to rank worker exposures relative to other workers in the cohort.

TABLE I. Number of Workers and Years of Operation of TCDD Contaminated Production Processes by Plant

Plant	Number of workers	NaTCP	2,4,5-TCP	2,4,5-Tacid	2,4,5-T-ester	2,4,5-Tamine	Silvex	Ronnel	Erbon	HCP
01	439	Feb 51–Aug 69		Feb 51–Aug 69	Feb 51–Aug 69	Feb 51–Aug 69				
03	665	Oct 57–Apr 79*		Oct 57–Apr 79*	Oct 57–Apr 79*	Oct 57–Apr 79*	Oct 71–Apr 79*			
04	355		Jan 57–Apr 59	Jan 57–Apr 59	Jan 57–Apr 59	Jan 63–Oct 78	Jan 64–Oct 78			
					Jan 63–Oct 78					
07	54				Aug 60–Jan 70					
08	202	Apr 48–Dec 69		Apr 48–Dec 69						
09	1408	Mar 42–Feb 79	Jan 46–Dec 72	Jan 48–May 71	Mar 50–Feb 79	Jan 50–Dec 83	Jan 58–Nov 78	Jan 55–Dec 74	Jan 55–Dec 74	
10	262	Jan 49–Jun 72	Jan 49–Jun 72							
11	153									Jan 50–May 84

*TCDD process operation was not continuous.
NaTCP = sodium 2,4,5-trichlorophenate, 2,4,5-TCP = 2,4,5-trichlorophenol, 2,4,5-Tacid = 2,4,5-trichlorophenoxyacetic acid, 2,4,5-Tester = 2,4,5-Tester produced from 2,4,5-Tacid, Silvex = 2-(2,4,5-trichlorophenoxy) propionic acid, Ronnel = 0,0-dimethyl-0-(2,4,5-trichlorophenyl) phosphorothioate, Erbon = 2-(2,4,5-trichlorophenoxy) ethyl 2,2-dichloropropionate, HCP = 2,2′-methylene-bis-(3,4,6-trichlorophenol) (hexachlorophene).

The TCDD exposure scores were computed by job and were plant, process, and calendar time specific. The cohort included only those workers at the plants with records of assignment to processes contaminated with TCDD. Detailed work history records were used to determine daily TCDD exposure scores for each worker in the cohort for all time periods the worker was assigned to TCDD contaminated process areas. Time worked in nonexposed areas was not counted. The sum of the daily exposure scores constituted an individual's cumulative exposure score.

Description of Algorithm Factors

Values were assigned to the algorithm factors for calendar time periods of exposure when conditions in a work area remained approximately constant. A new exposure time period was initiated whenever: 1) the concentration of TCDD in products, process streams and/or wastes changed; or 2) substantial documented changes took place in process operating conditions, engineering controls, or relative production volumes.

TCDD Concentration

Bulk sampling data describing the level of TCDD contamination in process materials were collected by NIOSH from the individual companies, several independent laboratories, the Department of Agriculture, and the Department of Defense [Woolson et al., 1972; Fee et al., 1975; Tiernan, 1976]. More than 12,000 sample results were obtained. Just over half of the analytical data came from Plant 9, which also contributed the greatest number of workers and years of operation of TCDD contaminated processes. As shown in Table II, the TCDD concentration varied between plants and over time. The level of TCDD contamination in TCP and TCP derivatives depended on process operating parameters, such as temperature, pressure and reaction time, and the level of purification. Plants 3, 9 and 10 reduced the concentration of TCDD in TCP through distillations and /or decantations, which resulted in TCDD being concentrated in the still bottoms and waste oils. The mean TCDD concentration in the still bottoms and waste oils ranged from 24 μg/g to more than 2,000 μg/g. Plant 1 installed an activated carbon filter in 1967 to reduce TCDD levels. Plants 4 and 11 primarily purchased purified TCP to produce derivatives. For all plants, the mean level of TCDD in TCP and derivatives ranged from 0.001 μg/g to 25 μg/g.

Arithmetic means of the TCDD sample results for a given process for a specific calendar time period were used to compute TCDD exposure scores [Seixas et al., 1988]. Sample results less than the limit of detection (LOD) were assigned one-half the limit of detection to estimate mean TCDD concentrations [Hornung et al., 1990]. The estimated mean TCDD concentrations for computing TCDD exposure

TABLE II. Bulk Sampling Data

Plant	Substance	Dates	# Samples (# non-detectable)	TCDD concentration (micrograms per gram) Mean*	Range	
1	Na 2,4,5-TCP	1965–1967	30	17.5	2.4	42
1	Na 2,4,5-TCP	1967–1969	31 (15)	0.64	0.45	2.8
1	2,4,5-T	1965–1966	15	18.6	5	50
1	2,4,5-T	1967	3	0.71	0.15	1.5
3	2,4,5-T	1965	24	1.9	0.4	3.3
3	2,4,5-T	1967–1970	8 (8)	0.09	—	—
3	2,4,5-T	1972–1979	610 (584)	0.05	0.009	2
3	Still bottoms	1978–1979	2	39	37.8	40
4	Na 2,4,5-TCP	1967–1968	12 (4)	0.2	0.7	1
4	Na 2,4,5-TCP	1971	148 (128)	0.8	0.1	3
4	Na 2,4,5-TCP	1972–1977	1,799 (1,763)	0.05	0.02	2.5
4	2,4,5-T/ester	1970	4	0.75	0.1	1.42
4	Silvex/ester	1970	17	2.8	0.9	9.5
4	2,4,5-T/ester	1971	142 (69)	0.86	0.1	7.4
4	Silvex/ester	1971	121 (25)	0.65	0.1	4
4	2,4,5-T/ester	1972	42 (24)	0.55	0.05	3.9
4	Silvex/ester	1972	148 (59)	0.56	0.1	7.7
4	2,4,5-T/ester	1973	110 (110)	0.05	—	—
4	Silvex/ester	1973	96 (76)	0.17	0.15	2.4
4	2,4,5-T/ester	1974–1977	446 (429)	0.05	0.01	0.25
4	Silvex/ester	1974–1977	83 (83)	0.05	—	—
4	2,4,5-T Formulations	1974–1977	167 (165)	0.05	0.01	0.2
7 and 8†	2,4,5-T	1958–1964	8	9.9	5	12
7 and 8†	2,4,5-T	1965	17	23	5	55
7 and 8†	2,4,5-T	1965	13	8.7	6.5	11
7 and 8†	2,4,5-T	1966	27	10.5	3	28
7 and 8†	2,4,5-T	1967	116 (8)	8.8	1	25
7 and 8†	2,4,5-T	1968	29 (12)	3.4	3	12
7 and 8†	2,4,5-T	1969	83	2	0.3	22
9	NaTCP	1964–1965	96 (23)	2.1	0.6	16
9	NaTCP decanted wastes	1962–1965	80	2,145	1.6	9,680
9	NaTCP decanted wastes	1966–1978	258 (15)	26.0	0.005	190
9	TCP still bottoms	1964–1965	21 (5)	688	5	3,600
9	TCP still bottoms	1966–1977	19	9.9	1.8	19
9	TCP	1964–1965	100 (89)	0.95	0.8	20
9	TCP	1967	183 (183)	0.5	—	—
9	TCP	1968	84 (84)	0.5	—	—
9	TCP	1970	57 (54)	0.28	0.63	1.3
9	TCP	1971	143 (65)	0.1	0.01	0.1
9	TCP	1972	251 (165)	0.02	0.01	0.1
9	TCP	1973–1978	1546 (1460)	0.007	0.0005	0.06
9	2,4,5-T	1965	109 (76)	0.66	1	3.1
9	2,4,5-T	1969–1973	115 (8)	0.11	0.05	0.44
9	2,4,5-Tester	1972–1978	3,450 (614)	0.05	0.001	2.8
9	Agent Orange	1966–1970	26 (26)	0.33	—	—
9	2,4,5-Tamine	1971—1978	61 (37)	0.02	0.01	0.07
9	Silvex	1970–1973	48 (31)	0.16	0.07	1.5

TABLE II. (*Continued*)

Plant	Substance	Dates	# Samples (# non-detectable)	TCDD concentration (micrograms per gram) Mean*	Range	
9	Silvex ester	1965–1978	101 (27)	0.03	0.01	0.18
9	Ronnel	1966	1	0.07	—	—
9	Ronnel	1967–1970	10 (10)	0.15	—	—
9	Ronnel	1973–1978	207 (195)	0.004	0.001	0.02
9	Erbon	1973–1975	102 (38)	0.04	0.004	0.22
9	Tordon	1974–1978	67 (6)	0.03	0.01	0.07
10	Crude TCP	1965–1970	5	25	12	47
10	Still Bottoms	1965–1970	2	362	230	494
10	TCP	1965	40 (40)	0.5	—	—
10	TCP	1970	9 (9)	0.07	—	—
10	TCP	1971—1976	27 (21)	0.01	0.001	0.032
11	TCP	1976–1983	142 (134)	0.001	0.001	0.004
11	HCP	1970–1971	23 (23)	0.01	—	—
11	HCP	1976–1977	213 (195)	0.001	0.001	0.004

*Mean of all samples, nondetectable results set to limit of detection/2.
NaTCP = sodium 2,4,5-trichlorophenate, 2,4,5-TCP = 2,4,5-trichlorophenol, 2,4,5-Tacid = 2,4,5-trichlorophenoxyacetic acid, 2,4,5-Tester = 2,4,5-Tester produced from 2,4,5-Tacid, Silvex = 2-(2,4,5-trichlorophenoxy) propionic acid, Ronnel = 0,0-dimethyl-0-(2,4,5-trichlorophenyl) phosphorothioate, Erbon = 2-(2,4,5-trichlorophenoxy) ethyl 2,2-dichloropropionate, HCP = 2,2′-methylene-bis-(3,4,6-trichlorophenol)(hexachlorophene).
†2,4,5-T produced at Plant 8 was esterified and formulated at Plant 7.

scores were less precise for TCP processes that included distillation or decantation than for other processes with less variability in the TCDD concentration. The mean TCDD concentrations used in the algorithm to compute exposure scores for routine process operations ranged from 0.001 to 350 μg/g TCDD.

Although TCP production began in the 1940s, analytic data for TCDD are available only for the later years of production, primarily from 1965 to 1983. In the mid-1960s, a vapor phase chromatography (VPC) method was developed which had detection limits around 1 part per million (ppm). Development of a gas chromatography/mass spectrometric (GC-MS) method dropped the limit of detection to the part per billion range in the 1970s [IARC, 1997; Marlow et al., 1991d].

For computation of TCDD exposure estimates for time periods before 1965, we used: 1) an estimated TCDD concentration based on rabbit ear tests for chloracnegens (Plant 9); 2) the TCDD concentration of archived samples (Plants 3 and 8); or 3) the TCDD concentration of process samples after 1964 when analytical data were available (all other plants).

As early as the 1940s, Plant 9 tested process samples in rabbit ears for chloracnegens and graded the development and severity of acnegenic activity from 0 to 4. After the development of TCDD analytical methods in the 1960s, Plant 9 chemists evaluated the grading scheme and found that TCDD contaminated process samples with grade 0 "no folliculitis" corresponded to a concentration of < 1 microgram TCDD per gram (μg/g), while grade 4 "severe folliculitis" developed at TCDD concentrations > 100 μg/g. Using the TCDD values for the acnegenic categories, information regarding changes in severity of response relative to process changes, and TCDD concentrations measured for the same process in the 1960s, we estimated TCDD concentrations for Plant 9 from 1942 until TCDD measurements were available in the 1960s. Analysis of archived samples at Plant 3 provided information on the level of TCDD contamination before major process changes occurred in 1965. Plant 8 had archived samples dating from 1958 that were useful for describing the level of TCDD concentration before 1965.

Interviews with plant personnel and review of process records indicated that most plants did not institute process changes to limit the level of TCDD contamination until the late 1960s. Therefore, TCDD measurements on samples of process materials taken before controls were instituted in the plants to reduce TCDD levels were used to compute TCDD exposure scores for production periods prior to 1965.

We were able to evaluate the TCDD data reported by five of the eight plants using results of TCDD analyses conducted for the Department of Defense (DOD) to characterize the TCDD content of Agent Orange stocks remaining after the Vietnam War [Fee et al., 1975; Tiernan,

TABLE III. Comparison of Plant and Department of Defense Analyses for TCDD

Source of analytical data	Substance analyzed	Production dates	Number of samples (# ND)	Mean TCDD concentration* micrograms per gram (standard deviation) Agent Orange	2,4,5-T
Plant 1					
Plant 1	2,4,5-T	1965–66	15	—	18.6 ($\pm$ 14.9)
Dept. of Defense	Agent Orange ASN 18‡	Not available	16 (1)	11.4 ($\pm$ 3.4)	22.8§
Dept. of Defense	Agent Orange ASN 11‡	Not available	30	6.3 ($\pm$ 2.2)	12.6§
Plant 3					
Plant 3	2,4,5-T	1967–70	8 (8)	—	< 0.2
Dept. of Defense	Agent Orange ASN 14‡	Not available	48 (44)	0.01	0.02§
Dept. of Defense	Agent Orange ASN 8‡	Not available	55 (55)	0.01	0.02§
Plants 7 and 8*					
Plant 8	2,4,5-T	1965	17	—	23 ($\pm$ 13.7)
Plant 8	2,4,5-T	1966	27	—	10.5 ($\pm$ 6.2)
Plant 8	2,4,5-T	1967	116 (8)	—	8.8 ($\pm$ 5.8)
Plant 8	2,4,5-T	1968	29 (12)		3.4 ($\pm$ 2.9)
Dept. of Defense	Agent Orange ASN 6‡	Not available	30	12.3 ($\pm$ 2.0)	24.6§
Plant 9					
Plant 9	Agent Orange	1966–1970	26 (26)	0.33	0.66§
Dept. of Defense	Agent Orange ASN 10‡	Not available	105 (2)	0.26 ($\pm$ 0.13)	0.52§

† Mean of all samples, non-detectables set to limit of detection/2 2,4,5-T = 2,4,5-trichlorophenoxyacetic acid.
‡ Analytical Sequence number identifying Agent Orange procurement.
§ TCDD concentration doubled to compare to 2,4,5-T/ester used to formulate Agent Orange.
*2,4,5-T produced at Plant 8 was esterified and formulated at Plant 7.

1976]. Plant 9 reported TCDD data for Agent Orange. However Plants 1, 3, 7, and 8, reported the level of TCDD in the 2,4,5-T used to produce Agent Orange. The TCDD concentration in Agent Orange was approximately half of the TCDD concentration in the 2,4,5-T that was esterified and formulated to Agent Orange. Agent Orange was a 50 : 50 mixture of the esters of 2,4,5-T and 2,4-dichlorophenoxy acetic acid (2,4-D), and 2,4-D did not contain TCDD. The TCDD concentrations reported for Agent Orange are provided in Table III and are doubled to allow a comparison to the plant data for 2,4,5-T. The independent analyses, conducted by a single contract laboratory for the Department of Defense, confirm the low TCDD concentrations reported for Plants 3 and 9, and the higher levels reported for Plants 1, 7 and 8 (Table III).

Contact Factor

To estimate the potential for contact with TCDD, job titles were grouped into seven broad categories, including production workers (64.7%), maintenance (21.5%), plant supervisors (2.8%), working supervisors (2.0%), engineers (1.6%), chemists (4.3%) and workers assigned to other processes adjacent to a TCDD process (proximity exposure—3.2%). Contact factors were used to estimate the relative difference in exposure due to job tasks based on the potential for dermal exposure and the inhalation of TCDD contaminated particulates. Job and process descriptions and industrial hygiene surveys were used to estimate the relative level of exposure among jobs by assessing factors associated with dermal exposure and absorption such as skin loading, the location and extent of skin surface area contamination, and frequency of contact [Grandjean, 1990; Wester and Maibach, 1991; Fenske, 1993]. A contact factor is also used to account for inhalation. Due to the low vapor pressure of TCDD (7.4×10^{-10} mm Hg at 25°C), inhalation of TCDD in the gaseous form was expected to have been low; however, there was the potential for exposure to airborne TCDD contaminated particulates for processes with drying, grinding and packaging operations.

Direct contact with process materials occurred during the operation of the process. Indirect contact also occurred when skin or clothing touched surfaces contaminated with TCDD from leaks, drips and spills in production areas and by the transfer of TCDD contamination from equipment and workers' gloves and clothes to other surfaces. Wipe sampling data collected at Plants 3, 9 and 11 showed TCDD contamination in production areas as well as other areas such as control rooms, offices, and lunch and locker rooms [Marlow et al., 1987, 1991; Piacitelli et al., 1991].

TABLE IV. Contact Factors

Indirect Contact Values	
0.01	Exceptional minimal contact assigned to workers adjacent to a TCDD process with documented safety and work practice precautions over and above other sites in the cohort.
0.05	Minimal contact with TCDD contamination from repeated contact with contaminated surfaces, wearing contaminated clothes or gloves. Assigned to adjacent production workers on non -TCDD contaminated process in a TCDD process area. Office and administrative tasks of plant and working supervisors, chemist and engineer.
0.10	Contact with TCDD contaminated equipment as well as area surfaces, contaminated clothes or personal protective equipment. Assigned to workers who alternately produced both non-TCDD product (2,4-D ester) using the same equipment used to produce TCDD product (2,4,5-T ester). Assigned to job duties outside process area for maintenance workers who maintained both TCDD and non-TCDD processes.
0.25	Contact due to the repair of contaminated process equipment in the shop, using contaminated tools, wearing contaminated clothes and gloves. Assigned to job duties outside the process area for maintenance workers who were primarily responsible for TCDD contaminated processes.
Direct Contact Values	
0.50	Moderate direct contact with process materials relative to production workers. Assigned to working supervisors, chemists, engineers typically exposed to smaller amounts of process materials than production workers over limited skin surface area (e.g. hands and arms), some exposure to greater amount of materials over larger skin surface but less routinely than production workers.
0.75	Production work in state of art process built to reduce worker exposure.
1.0	Production and maintenance work had the potential for repeated direct contact with TCDD contaminated process materials on a routine basis, exposed skin area could include the face, head, neck, arms, hands, torso, legs, and feet.
1.25	Exceptional direct contact due to manually intensive tasks done on a routine basis that had the potential for contact with greater amount of TCDD contaminated materials over larger area of body. Assigned to jobs involving manual transfer of material such as shoveling TCDD contaminated process materials, and digging out centrifuges. Also assigned to cleanup of TCDD released during TCP reactor explosions.
1.50	Production work with exposure to TCDD contaminated dusts due to drying, grinding, packaging operations.

Production workers had repeated opportunity for contacting TCDD contaminated material while operating the process. Tasks such as collecting samples, mixing and transferring process materials, drumming product, cleaning vessels and spills as well as unplugging lines had the potential for repeated dermal contact of the hands and could include arms, head, neck, legs, and feet. The level of contact for routine production work was set to 1. All other assessments were made relative to this value. A range of eight contact factors (0.01, 0.05, 0.1, 0.25, 0.5, 0.75, 1.0, 1.25) was used to account for different levels of dermal exposure due to skin loading, location and extent of skin surface area contamination, and frequency of contact based on job duties. An additional factor (1.5) was used to account for exposure to TCDD contaminated particulates. These contact values are based on industrial hygiene judgment and are described in Table IV.

Time Exposed

Exposure was estimated per workday. Production workers were assigned a full day duration (a value of 1) in the process area with the opportunity for repeated contact with TCDD on a routine basis. Production support personnel, such as working supervisors and engineers, had process related duties and as well as other duties indirectly associated with the process. Job duties and exposure descriptions were used to time-weight exposure by intensity using contact level factors (Table V).

Some workers were responsible for multiple processes or products, which were not all contaminated with TCDD. The exposure assignments were adjusted to reflect time spent with direct exposure to TCDD. For example, ester operators used the same equipment to make both 2,4,5-T esters (which contained TCDD) and 2,4-D esters (which did not contain TCDD). Their exposure was computed by time weighting TCDD exposure by relative production volume estimates which ranged from 20% to 100% 2,4,5-T esters. Some workers had jobs that spanned multiple processes, not all of which were contaminated with TCDD but were typically located in the same building. These workers were assumed to have worked an equal amount of time on each process, but were assigned different contact levels to account for exposure due to direct contact while working on a TCDD process and indirect contact while working on an adjacent process.

Example Computations of TCDD Exposure Scores

Table VI provides examples of computations of the daily TCDD exposure scores for a sample of job titles assigned to the 2,4,5-T process building at Plant 9 for the exposure time period 1948 to 1966. The TCDD concentra-

TABLE V. Time-weighted Contact Assignments

Maintenance Workers	Maintaining and cleaning process equipment, fixing leaks and spills, repairing pumps, conveyors, lines and equipment resulted in dermal contact. Indirect exposure occurred from repair of contaminated equipment in shop, using contaminated tools, and wearing contaminated clothes. Maintenance workers at Plants 3 and 9 were assigned 75% of a day at a direct contact value of 1; and 25% of a day at the indirect contact value of 0.25. Maintenance workers at Plants 1 and 4 were estimated to spend 40% of their time maintaining TCDD processes, while at Plant 10 repairmen were estimated to spend 10% of their time maintaining a TCDD process. Maintenance workers at Plant 10 who had less direct exposure were assigned a lower indirect contact value of 0.1 to account for relatively less TCDD contamination of shop, tools etc.. Maintenance workers at Plants 7, 8 and 11 could not be linked to TCDD processes and therefore were excluded.
Chemist	Contact with TCDD process materials occurred while handling samples, running tests, cleaning glass ware etc.. Chemists had relatively less extensive contact than production worker due to exposure to smaller amounts of process materials over a smaller skin surface area, primarily hands and arms. They were assigned 50% of the day at direct contact value of 0.5, and 50% of the day at the minimal indirect contact level of 0.05 while performing office duties, recording results and preparing reports.
Engineer	50% of the time in process area supervising operations, trouble shooting, collecting samples, making and evaluating process improvements. Moderate contact with process materials relative to production workers, assigned a contact level of 0.5. Remaining 50% of day at minimal indirect contact of 0.05 for administrative and office duties, office often in process building.
Working Supervisors	75% of the day overseeing process operations, trouble shooting, and providing relief to production workers at an average contact level of 0.5, remainder of the day (25%) performing office and administrative duties at indirect contact level of 0.05.

TABLE VI. Examples of Daily TCDD Exposure Score Computations by Plant and Job Category

	Applicable exposure time period		Daily TCDD exposure						
			Direct exposure			Indirect exposure			
Plant and job	**Begin date**	**End date**	**TCDD conc (μg/g)**[¶]	**Time (fraction of day)**	**Contact level (0–1.5)**	**TCDD conc (μg/g)**[¶]	**Time (fraction of day)**	**Contact level (0–1.5)**	**Daily TCDD exposure score (direct+indirect)**[‡]
Plant 9 - 2,4,5-T process									
2,4,5-T operator	Jan 1948	May 1966	0.66	1	1	—	—	—	0.66
Maintenance	Jan 1948	May 1966	0.66	0.75	1	0.66	0.25	0.25	0.54
Chemist	Jan 1948	May 1966	0.66	0.5	0.5	0.66	0.5	0.05	0.18
Plant 1 - 2,4,5-T process									
2,4,5-T operator	Feb 1951	Aug 1967	18.6	1	1	—	—	—	18.6
2,4,5-T operator	Sept 1967	Aug 1969	0.71	1	1	—	—	—	0.71

[‡] Daily TCDD exposure score = sum of direct exposure (TCDD concentration × Time × Contact) and indirect exposure (TCDD concentration × Time × Contact).
[¶] Applicable plant, department and time specific TCDD concentration in micrograms per gram of process material.

tion for this exposure period was 0.66 μg/g based on the analysis of 109 samples of 2,4,5-T analyzed by Plant 9 in 1965. Job duties and exposure descriptions were used to time-weight exposure by intensity using direct and indirect contact level factors. For this process, 2,4,5-T operators were assigned the highest exposure score of 0.66, maintenance workers scored slightly lower with a score of 0.54, with the lowest exposure score of 0.18 assigned to chemists. To illustrate plant and time period differences, the exposure scores for 2,4,5-T reactor operators at Plant 1 are provided for the exposure time period from 1951 to August 1967 and for a second exposure time period, September 1967 to August 1969. Following the addition of a charcoal filter in September 1967 to reduce the TCDD concentration, the TCDD exposure score for 2,4,5-T operators at Plant 1 dropped from 18.6 to 0.71 μg/g, which was similar to the Plant 9 score where purified TCP was also used to produce 2,4,5-T. For each worker, work history records were used to assign the appropriate daily score. The daily scores were accumulated over time to give a cumulative exposure score.

ACCIDENTS

Major incidents involving TCDD exposure occurred at Plants 3, 4, and 8. Runaway reactions in the TCP reactors resulted in the rapid increase of temperature and pressure with the explosive release of reactor contents. These higher temperatures and pressures also resulted in the increased formation of TCDD. However, there are no analytical data describing the level of TCDD associated with any of these incidents, which occurred in 1948 (Plant 8), 1959 (Plant 4) and 1974 (Plant 3). An incident also occurred at Plant 1, but worker exposure to TCDD was considered to be limited because the reactor contents were released into a river prior to the explosion and fire.

Although there are no analytical data describing TCDD concentrations associated with these accidents, serum TCDD levels were obtained between 1988 and 1992 for 138 workers who had been involved in the assessment, clean-up and demolition activities following a TCP reactor accident that occurred in Ludwigshafen, Germany in 1953 [Ott et al., 1993]. The serum TCDD levels and duration of individual exposure and descriptions of the circumstances of exposure were used by the authors in a regression model to evaluate the relationships between various exposure situations and TCDD concentrations. Based on modeling results and TCDD elimination rates, the authors concluded that the exposure intensities for workers exposed during the first 22 days after the accident were estimated to be 1000 times higher than for production employees who worked in the building after an extensive cleanup had occurred and produced products other than TCP; no TCDD contaminated processes.

The exposure intensity reported for the German clean-up workers was used as a guide to estimate the TCDD exposure of the U.S. workers involved in accidents in order to rank their exposure relative to the other workers in the cohort. An accident concentration of 1,000 μg/g was used to estimate the exposure of workers involved in the accident at Plant 8. The accident at Plant 8 was similar to the accident in Ludwigshafen, Germany [Theiss et al., 1982]. The incidents at Plants 3 and 4 appeared to be of less magnitude with respect to TCDD exposure than at Plant 8. At Plant 3, the runaway reaction was relieved by the release of the reactor contents to a holding dike, which subsequently caught fire. At Plant 4, a rapid pressure increase in the TCP reactor resulted in an explosion followed by a fire that destroyed the plant. The available descriptions of the accidents suggest that the runaway reaction period was shorter for Plants 3 and 4 than for Plant 8; therefore, potentially less dioxin was formed. In addition, the fires that occurred at Plants 3 and 4 may have reduced the concentration of TCDD formed due to thermal destruction. At Plant 8 the pressure build up was inadequately relieved through a hand vent and an emergency vent, the reaction continued until one of the vents twisted off and the reactor contents were sprayed over the building; no fire was involved. The TCDD concentration assigned to the clean-up periods for Plants 3 and 4 was 100 μg/g TCDD, which was an order of magnitude lower than the concentration estimated for Plant 8. In addition to higher TCDD

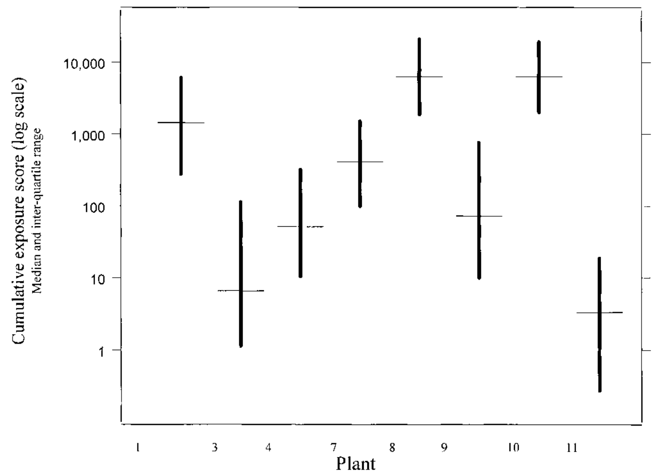

FIGURE 1. Cumulative exposure score by plant.

concentrations, the contact level was increased to 1.25 due to increased potential for skin exposure for workers involved with clean up. TCDD exposure resulting from accidents was assigned to a total of 47 workers (1% of the cohort), who were identified by plant records.

RESULTS

Daily TCDD exposure scores were determined by job and were plant and calendar time specific. The daily scores ranged from 0.001 to 1,250. Work history records were used to compute cumulative exposure scores by summing the individual's daily scores during periods exposed to TCDD over his entire work history. Cumulative exposure scores ranged from 0.002 to 1,559,430. Figure 1 shows the wide distribution of the cumulative TCDD exposure score (median and 25–75% range) by plant.

No gold standard exists to validate the exposure matrix and the TCDD exposure scores. However, records of chloracne status at eight plants and serum TCDD levels for 193 of 439 workers at Plant 1 were used to evaluate the exposure scores. Chloracnegenic response has generally been considered to be due to relatively high exposure, although the absence of chloracne does not imply a lack of exposure to TCDD. NIOSH reviewed records for each of the eight plants and identified 393 workers (11% of the exposure matrix cohort) who had chloracne during their employment. The median cumulative TCDD exposure score for the 393 workers with chloracne is 11,546 versus a median of 77 for the 3,145 workers without chloracne. This marked difference persisted when the cumulative TCDD exposure score was divided by duration of exposure (in days) to obtain the average daily exposure score (10.0 vs. 0.3). The inter-quartile (25–75%) range of cumulative exposure scores for those workers with chloracne was from 2,950 to 34,490 versus 6.8 to 1000 for those workers without records of chloracne.

Serum TCDD levels and cumulative exposure scores are only available for 193 workers at Plant 1 who participated in a medical study in 1987–1988 [Sweeney et al., 1990]. Occupational exposure for Plant 1 workers occurred between 15–37 years before the serum samples were collected; therefore, the levels were back-extrapolated to each worker's date of last exposure. The mean of the back-extrapolated serum TCDD levels for 193 of 439 workers at Plant 1 was 2,481 parts per trillion (ppt), with a range from 2 to 32,347 ppt. The Spearman Correlation Coefficient between cumulative exposure score and serum level was 0.70, and between duration and serum level it was 0.74. The exposure scores did not improve upon duration of exposure as an estimate of exposure level at this plant, probably because detailed information regarding process assignment was limited in the work history records. In addition, for 16 of the 18 years of operation, NaTCP was not purified and therefore there was little difference between the TCDD concentration in NaTCP and NaTCP derivatives. However, there were other non-TCDD contaminated processes at the plant and many job titles did not specify process assignment. According to surveys conducted at the site there was considerable job rotation and workers often worked in several locations [Birmingham et al., 1963; Poland et al.,1971]. For this plant we had limited ability to assess differences in exposure level as shown by the Spearman correlation coefficient between cumulative exposure score and duration which was 0.91. This was not the case for the overall cohort, the Spearman correlation coefficient between cumulative exposure score and duration was 0.60, indicating differences in the intensity of exposure due to differences in the level of TCDD contamination, level of contact and time exposed. It should be noted that the serum TCDD measurements are not a perfect gold standard, due in part, to the timing of collection of the serum samples, which were collected between 15–37 years after the workers were last employed in TCDD contaminated jobs. In addition, a standard half-life of 8.7 years was used to back-extrapolate although half-life can vary appreciably between individuals due to percent body fat and other individual characteristics [Michalek et al., 1996].

DISCUSSION

Exposure was evaluated indirectly using the time assigned to TCDD process areas, the level of TCDD contamination in process materials, and the degree of contact with contaminated materials based on job duties. We do not know what fraction of TCDD was transferred to the skin from contact with process materials and surface contamination nor what fraction was absorbed via dermal penetration, ingestion or inhalation. Although, we cannot quantify dose, the algorithm provides a consistent method for quantitatively describing exposure as a score that allows the ranking of workers in the cohort relative to each other. It is the relative ranking of exposure which is important for exposure–response analyses.

As with any retrospective effort to quantify exposure, this exposure assessment has a number of limitations. Although exposure for some workers occurred as early as the 1940s, the earliest analytical data is from 1958, with most plants having data beginning in the mid to late 1960s. In addition, measurements were fairly sparse for some plants and some process materials. However, the data from the acnegenic testing of process materials at Plant 9, the archived samples for Plants 3 and 8, process records and worker interviews provided a framework to estimate TCDD concentrations for the early production periods. We were able to assess the quality of the analytical data for five of the eight plants using TCDD analyses of Agent Orange stocks which showed reasonable agreement with the TCDD concentrations reported by the plants.

Differences in exposure due to potential vehicle effects (e.g., exposure to TCDD in TCP versus TCDD in 2,4,5-T) and individual factors of work practice and personal hygiene could not be addressed. It was not possible to assess retrospectively the use or efficacy of personal protective equipment (PPE). Contamination can get through or around openings of gloves and clothing [Fenske, 1988; Van Rooij et al., 1993] and contaminated PPE can be a source of exposure to workers [Quinlan et al., 1995]. In addition, although PPE has the potential for reducing exposures, it also has the potential for increasing dermal uptake through the skin due to increased penetration because of elevated skin temperature, humidity, and physical stress [Grandjean, 1990; Wester and Maibach, 1991].

Due to the large size of the original cohort, it was possible to limit the exposure matrix cohort to only those plants with the best information to characterize exposure, yet still have a sizeable cohort to study (n = 3538). It is important for the evaluation of possible exposure–response relationships that there are groups of workers with substantially different exposure levels. The analytical data from more than 12,000 samples shows a wide range of TCDD concentration in process streams, products, and waste. The substantial plant records permitted design of a job exposure matrix to account for differences in exposure among workers due to the range of TCDD concentration in process materials, duration in exposed jobs, and differences in potential contact with TCDD contaminated materials. Comparison of the cumulative TCDD exposure scores with chloracne status suggests that the matrix is reasonable and reflects the inter- and intra-plant and calendar time specific differences in exposure. The TCDD cumulative exposure scores, that permitted the relative ranking of worker exposures, have been used to evaluate exposure–response relationships between TCDD exposure and mortality in an updated cohort study analysis [Steenland et al., 1999].

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REFERENCES

Birmingham DJ, Key MM. 1963. Dermatological Investigation Report: Diamond Alkali Company, Newark, New Jersey. Occupational Health Research and Training Facility, Division of Occupational Health, Public Health Service, U.S. Dept. of Health, Education and Welfare, Cincinnati, Ohio.

Far HS, Pin NT, Kong CY, Fong KS, Kian CW, Yan CK. 1993. An evaluation of the significance of mouth and hand contamination for lead absorption in lead-acid battery workers. Int Arch Environ Health 64:439–443.

Federal Register. 1979a. Decision and emergency order suspending registration for the forest, rights-of-way, and pasture uses of 2,4,5-T. Fed Regist 44:15874, March 15, 1979.

Federal Register. 1979b. Decision and emergency order suspending registrations for certain uses of silvex. Fed Regist 44:15897, March 15, 1979.

Federal Register. 1983. 2,4,5-T and silvex products; intent to cancel registrations of pesticide products containing 2,4,5-T and silvex; revocation of notices of intent to hold a hearing to determine whether certain uses of 2,4,5-T or silvex should be canceled. Fed Regist 48(202):48434, October 18, 1983.

Fee DC, Huges BM. 1975. Analytical methods for herbicide orange, Vol. II: determination of origin of USAF stock. USAF ARL 75-001100. Vol. II.

Fenske RA. 1988. Comparative assessment of protective clothing performance by measurement of dermal exposure during pesticide applications. Appl Ind Hyg 3(7):207–213.

Fenske RA. 1993. Dermal exposure assessment techniques. Ann Occup Hyg 37(6):687–706.

Fingerhut MA, Blade L, Marlow D. 1984. Dioxin registry site visit report of Rhone Poulenc, Inc., Portland, Oregon. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.14, Reproduced by the U.S. Department of Commerce, National Technical Information Service Report No. PB 84-240035.

Fingerhut M, Halperin W, Marlow D, Piacitelli L, Honchar P, Sweeney MH, Greife A, Dill P, Steenland K, and Suruda A. 1991. Cancer mortality in workers exposed 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). N Engl J Med 324:212-218.

Grandjean P. 1990. Skin penetration: Hazardous chemicals at work. London, U.K.: Taylor and Francis.

Hornung RW, Reed LD. 1990. Estimation of average concentration in the presence of nondetectable values. Appl Occup Environ Hyg 5(1):46–51.

IARC. 1997. IARC Monogr Eval Carcinog Risk Hum, Vol. 69, Polychlorinated dibenzo-*para*-dioxins and polychlorinated dibenzofurans. Lyon: WHO, International Agency for Research on Cancer.

Karita K, Shinozaki T, Tomita K, Yano E. 1997. Possible oral lead intake via contaminated facial skin. Sci Total Environ 199:125–131.

Marlow DA, Fingerhut MA. 1984. Dioxin registry site visit report of Occidental Chemical Corporation, Hooker Chemical Center, Niagra Falls, New York. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report Number 117.18. Reproduced by the U.S. Department of Commerce, National Technical Information Service, Report No. PB 85-221786.

Marlow DA, Fingerhut MA. 1986. Dioxin registry report prepared by review of documents from Diamond Shamrock Corporation, Diamond Alkali Company, Newark, New Jersey. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.16. Reproduced by the U.S. Department of Commerce, National Technical Information Service, Report No. PB 87-222808.

Marlow DA, Fingerhut MA, Sweeney MH, Honchar P, Hearn S, Jones J. 1987. Dioxin registry site visit report of Syntex (USA). National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.11. Reproduced by the U.S. Department of Commerce, National Technical Information Service, Report No. PB 88-125992.

Marlow DA, Fingerhut MA, Piacitelli LA. 1989. Dioxin registry site visit report of Monsanto Company, Nitro, West Virginia. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.20. Reproduced by the U.S. Department of Commerce, National Technical Information Service Report, No. PB 91-107961.

Marlow DA, Fingerhut MA, Blade LM, Hearn S. 1990. Dioxin registry report prepared by review of documents received from: Thompson-Hayward Chemical Company, Kansas City, Kansas. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.12.

Marlow DA, Fingerhut MA. 1991a. Dioxin registry site visit report of Amchem Products, Inc., Ambler, Pennsylvania. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report Number 117.21. Reproduced by the U.S. Department of Commerce, National Technical Information Service Report No. PB 92-121599.

Marlow DA, Fingerhut MA. 1991b. Dioxin registry report for Thompson Chemical Company, St. Louis, Missouri. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.24. Reproduced by the U.S. Department of Commerce, National Technical Information Service Report No. PB92-121615.

Marlow DA, Fingerhut MA, Blade LM, Hearn S, Jones J. 1991c. Dioxin registry report for Hercules, Inc., and Vertac Chemical Corporation, Jacksonville, Arkansas. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.10.

Marlow DA, Fingerhut MA, Blade LM, Piacitelli LA, Roberts D. 1991d. Dioxin registry report of The Dow Chemical Company, Midland, Michigan. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report Number 117.15. Reproduced by the U.S. Department of Commerce, National Technical Information Service Report No. PB 92-121557.

Marlow DA, Fingerhut MA, Piacitelli LA. 1997. Dioxin registry site visit report of Monsanto Company, Sauget, Illinois. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.23.

Michalek M, Pirkle J, Caudill S, Tripathi R, Patterson D, Needham L. 1996. Pharmacokinetics of TCDD in veterans of Operation Ranch Hand: 10 year follow-up. J Toxicol Environ Health 47:209–220.

Ott GM, Messerer P, Zober A. 1993. Assessment of past occupational exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin using blood lipid analyses. Int Arch Occup Environ Health, 65:1–8.

Piacitelli LA, Marlow DA, Fingerhut MA. 1990. Dioxin registry site visit report of Givaudan Corporation, Clifton, New Jersey. National Institute for Occupational Safety and Health, Industry Wide Studies Branch Report No. 117.22. Reproduced by the U.S. Department of Commerce, National Technical Information Service, Report No. PB 91-185199.

Poland AP, Smith D, Metter G, Possick P. 1971. A health survey of workers in a 2,4,-D and 2,4,5-T Plant. Arch Environ Health 22: 316–322.

Quinlan R, Kowalczyk G, Gardiner K, Calvert I. 1995. Exposure to polycyclic aromatic hydrocarbons in coal liquefaction workers: impact of a workwear policy on excretion of urinary 1-hydroxypyrene. Occup Environ Med 52:600–605.

Roels H, Buchet J-P, Truc J, Croquet F, Lauwerys R. 1982. The possible role of direct ingestion on the overall absorption of cadmium or arsenic in workers exposed to CdO or As_2O_3 Dust. Am J Ind Med 3:53–65.

Seixas NS, Robins TR, Moulton LH. 1988. The use of geometric and arithmetic mean exposures in occupational epidemiology. Am J Ind Med 14:465–477.

Steenland K, Piacitelli L, Deddens J, Fingerhut M, Chang L. 1999. Cancer, heart disease and diabetes in workers exposed to 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Natl Cancer Inst 91:779–786.

Sweeney MH, Fingerhut MA, Patterson Jr. DG, Connally LB, Piacitelli LA, Morris JA, Greife AL, Hornung RW, Marlow DA, Duple JE, Halperin WE, Needham LL. 1990. Comparison of serum levels of 2,3,7,8-TCDD in TCP production workers and in an unexposed comparison group. Chemosphere 20 (7–9):993–1000.

Theiss AM, Frentzel-Beyme R, Link R. 1982. Mortality study of persons exposed to dioxin in a trichlorophenol-process accident that occurred in the BASF AG on November 17, 1953. Am J Ind Med 3:179–189.

Tiernan TO. 1976. Analytical and chemical support for herbicide disposition activities. Quarterly Report, November 15, 1975 to February 15, 1976. Wright State Univ., Dayton OH. U.S. Air Force, Directorate of Procurement and Production, San Antonio Air Logistics Center, Kelly Air Force Base, contract no. F41608-76-C-0464.

Ulenbelt P, Lumens M, Geron H, Herber R, Broersen S, Zielhuis R. 1990. Work hygienic behavior as modifier of the lead air-lead blood relation. Int Arch Environ Health 62:203–207.

Van Rooij JGM, Van Lieshout EMA, Bodelier-Bade MM, Jongeneelen FJ. 1993. Effect of the reduction of skin contamination on the internal dose of creosote workers exposed to polycyclic aromatic hydrocarbons. Scand J Work Environ Health 19:200–207.

Wester RC, Maibach HI. 1991. in vivo percutaneous absorption. In: Marzulli FN, Maiback HI, editors. Dermatoxicology, Fourth edition, New York: Hemisphere Publishing Corporation, pp 75–81.

Woolson EA, Thomas RF, Erson PD. 1972. Survey of polychlorodibenzo-p-dioxins content in selected pesticides. J Agric Food Chem 20(2):351–354.