The Dow Chemical Company
Midland, Michigan 48674

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(Attn: TSCA Section 8(e) Coordinator)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: Update of Previous Dioxin Mortality Study,
8EHQ-0398-14151

Dear Sir/Madam:

The following information is being submitted by The Dow Chemical Company (Dow) pursuant to current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act. Dow has made no determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

Submission 8EHQ-0398-14151 provided information from a probe study preliminary to a subsequent study designed to validate exposure estimates from Dow health studies of chemical workers potentially exposed to dioxins at one manufacturing facility. The report of the subsequent study is enclosed. The probe study is published and cited as Reference Number 1 in this final report.

Questions may be addressed to the undersigned.

Sincerely,

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CHLORINATED DIOXIN LEVELS AMONG WORKERS WITH TRICHLOROPHENOL AND PENTACHLOROPHENOL EXPOSURES

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Introduction

We examined the levels of 2,3,7,8-substituted chlorinated dioxins and furans, and 4 PCB congeners in the serum of former workers engaged in the production of 2,4,5 trichlorophenol (TCP) and pentachlorophenol (PCP). We compared these serum dioxin, furan and PCB levels to levels of workers at the same plant without potential for TCP and PCP exposures. We present the dioxin and furan profiles for our TCP and PCP workers and demonstrate how distinct the dioxin "fingerprints" are for these chlorophenols many years after workplace exposures.

Materials and Methods

Previously, we reported analogous results of 98 workers.[1] In the present study, we surveyed an additional 419 workers at the same site from which 314 (75%) agreed to participate. The overall participation rate was 76% (412 of 545) for the combined surveys. As in the previous study, all study candidates lived within 50 miles of The Dow Chemical Company plant in Midland, Michigan and worked in departments that used or produced TCP or PCP. All the results described in this report represent the combined study population of 412 workers. Participants were classified into one of 5 exposure groups: chlorophenol workers with only PCP exposure (85 workers), chlorophenol workers with only TCP exposures (237 workers) chlorophenol workers with both TCP and PCP exposures (43 workers), tradesmen who had plant-wide exposures (10 workers), and workers with no workplace chlorophenol exposure (37 workers). We subsequently refer to these five groups as PCP-only, TCP-only, PCP and TCP, tradesmen, and the referents. We calculated mean serum dioxin, furan and PCB levels and the 25% and 75% quartiles for each group and the total Toxic Equivalency (TEQ). At a company medical facility, we collected 80 milliliters of blood from each participant, allowed the blood to clot for 20 minutes, and then centrifuged the blood for 15 minutes at 2,500 rpm. The serum was transferred to rinsed glass vials and stored at -20^0C until laboratory analysis using high resolution gas chromatography/mass spectrometry at Alta Analytical following previously described procedures.[1] All results were lipid adjusted.

Results and Discussion

Table 1 presents the mean lipid adjusted dioxin, furan, and PCB levels for the four exposed groups and the referent group. Compared to referents, workers in the TCP-only group had significantly higher 2378-TCDD, 23678-H_6CDF, and 123789-H_6CDF levels, and total TEQ level. The distribution of the 2378-TCDD levels among the TCP-only workers and the referents are shown in Figure 1. While most of the referent group has 2378-TCDD levels below 10 ppt, the TCP-only workers have levels up to 175 ppt. Although serum levels of two furans were significantly higher than the referent group, the differences were very small. The remaining dioxins, furans and PCBs among the TCP-only workers were similar to the referent group .The TCP-only workers had the lowest average total TEQ value of all exposed workers, 52.3 ppt, compared to 32.8 ppt for the referent group.

Workers in the PCP-only group had levels of 123478-H_6CDD, 123678-H_6CDD, 123789-H_6CDD, 1234678-H_7CDD, and OCDD, plus total TEQ levels significantly higher than the referent group. Serum 12378-P_5CDD was also somewhat higher than in the referent group although this difference was not statistically significant. We used 123678-H_6CDD as a marker of PCP exposures. All furans and the PCB levels among PCP-only workers were similar to the referent group. The distributions of 123678-H_6CDD levels for PCP-only workers and referents are shown in Figure 2. While 78% of the referent group had 123678-H_6CDD levels below 100 ppt, almost half (49%) of PCP-only workers had levels above 100 ppt.

Compared to referents, workers with both PCP and TCP exposures experienced significantly higher 12378-P_5CDD, 123478-H_6CDD, 123678-H_6CDD, OCDD, and total TEQ levels. Levels of 2378-TCDD, 123789-H_6CDD, and 1234678-H_7CDD were about twice as high as in the referent group but these differences were

not statistically significant. This group had a mean total TEQ value (65.9 ppt) higher than either the TCP-only workers (52.3 ppt) or the PCP-only workers (57.4 ppt), but levels of furans and the PCBs were similar to the referent group. The Tradesmen had mean 12378-P_5CDD, 123478-H_6CDD, 23478-P_5CDF, 123478-H_6CDF, 123678-H_6CDF, PCB169, and total TEQ levels significantly higher than the referent group. Though not significantly different, levels of 123678-H_6CDD, 123789-H_6CDD, 1234678-H_7CDD, OCDD, and PCB126 were also 5.2 times (OCDD) to 1.8 times (PCB126) higher than the referent group. The average total TEQ level for tradesmen was the highest of all exposed groups.

Table 1. Mean lipid adjusted (pg/g lipid) serum levels of 2,3,7,8 substituted dioxins, furan, and PCB levels for four exposure group and the referents.

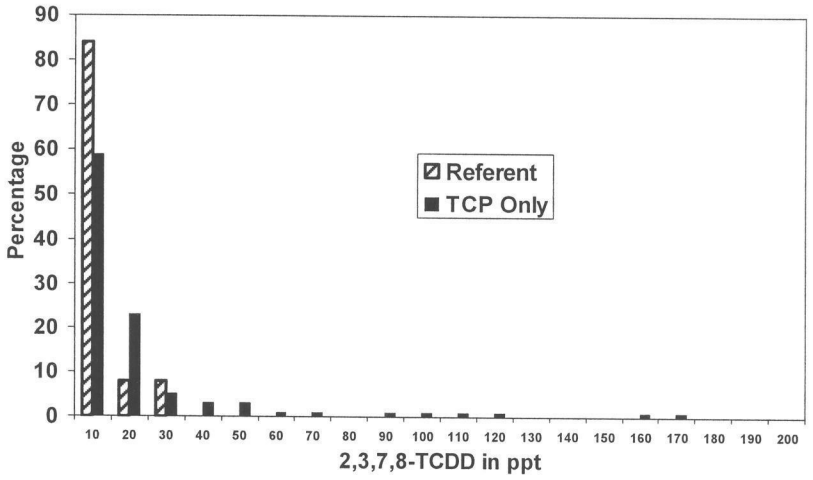
Congeners	Mean Lipid Adjusted Serum Concentration (25% and 75% Quintiles)				
	TCP-only Workers	PCP-only Workers	TCP & PCP Workers	Tradesmen	Referent Group
2378-TCDD	15.9* (3.7-16.2)	8.0 (3.5-9.7)	13.9 (4.2-14.5)	20.7 (10.1-24.1)	6.5 (2.4-8.2)
12378-P_5CDD	14.1 (8.0-16.8)	17.2 (9.8-20.0)	20.0* (9.4-19.5)	31.7* (18.4-39.3)	11.8 (6.5-14.7)
123478-H_6CDD	10.1 (5.8-12.3)	16.1* (8.1-16.3)	15.2* (6.9-14.5)	21.5* (8.6-34.2)	7.5 (4.9-10.2)
123678-H_6CDD	78.1 (47.6-94.6)	150.6* (74.0-157.0)	161.2* (57.4-129.0)	150.4 (77.0-211.0)	74.7 (46.5-96.2)
123789-H_6CDD	10.5 (6.2-12.6)	20.2* (7.0-21.0)	16.0 (6.9-19.9)	21.0* (6.3-33.7)	8.6 (5.2-11.0)
1234678-H_7CDD	69.1 (35.4-86.5)	192.6* (41.0-161.0)	148.7 (40.8-146.0)	264.4* (46.2-299.0)	68.7 (47.1-88.9
OCDD	616.2 (264-728)	2594.0* (459-2390)	2331.5* (361-1560)	2502.6 (683-2650)	509.1 (270-677)
2378-TCDF	0.6 (0.2-0.6)	0.5 (0.2-0.6)	0.4 (0.2-0.5)	0.6 (0.2-0.9)	0.6 (0.3-0.6)
12378-P_5CDF	1.2 (0.3-1.5)	0.8 (0.3-1.3)	0.8 (0.3-0.9)	0.7 (0.2-1.0)	0.6 (0.3-0.7)
23478-P_5CDF	10.6 (6.8-14.1)	10.1 (7.1-12.7)	10.4 (7.3-12.8)	15.2* (10.9-19.9)	9.6 (6.2-11.4)
123478-H_6CDF	7.1 (4.5-8.7)	10.2 (6.7-13.2)	11.3 (7.1-15.2)	13.7* (6.6-18.9)	7.7 (5.5-10.0)
123678-H_6CDF	9.9* (6.3-12.1)	10.1 (6.5-12.2)	9.6 (6.2-11.0)	12.0* (7.0-15.6)	7.5 (5.2-9.6)
234678-H_6CDF	1.6 (0.8-2.0)	1.8 (0.7-2.4)	1.9 (0.8-2.7)	1.9 (0.5-2.9)	1.6 (1.0-2.5)
123789-H_6CDF	0.8* (0.5-1.1)	0.7 (0.4-1.0)	0.8 (0.5-1.0)	0.6 (0.4-0.7)	0.5 (0.2-0.4)
1234678-H_7CDF	10.9 (6.4-12.0)	13.5 (6.6-14.7)	12.3 (6.2-16.7)	14.5 (10.8-17.8)	11.1 (7.7-13.4)
1234789-H_7CDF	0.7 (0.4-0.8)	0.7 (0.4-0.8)	0.6 (0.4-0.8)	0.6 (0.4-0.9)	0.7 (0.3-0.6)
OCDF	2.1 (1.3-2.5)	2.3 (1.3-2.8)	1.8 (1.3-2.1)	2.1 (1.4-2.5)	4.6 (1.2-2.4)
PCB77	7.2 (3.3-6.0)	4.5 (2.9-5.4)	5.2 (3.0-6.2)	4.2 (2.6-5.6)	4.9 (2.6-5.0)
PCB81	2.5 (1.0-3.0)	2.1 (1.0-2.4)	2.4 (0.9-2.7)	2.3 (1.0-2.9)	2.1 (0.8-2.3)
PCB126	37.1 (14.8-46.3)	33.5 (13.6-44.9)	30.5 (13.6-42.2)	49.8 (14.8-88.4)	29.2 (14.8-34.8)
PCB169	47.7 (29.4-59.6)	40.9 (27.5-50.0)	45.9 (29.3-59.1)	64.8* (51.4-75.4)	43.3 (25.9-45.0)
TEQ-WHO	52.3*	57.4*	65.9*	90.8*	38.2
Workers	237	85	43	10	37

* Significantly different than the referent group at $p<0.05$ using a t-test.

The evaluation of 375 exposed workers and 37 referents makes this serum dioxin evaluation to our knowledge the largest ever done on production workers exposed to chlorophenols. We found distinctly different "fingerprints" for TCP and PCP workers. Consistent with several other studies,[2-6] we have found

that TCP workers have increased levels of 2378-TCDD and no other dioxin or furan congeners are increased in TCP workers. While some studies of TCP exposed persons do report higher 12378-P_5CDD levels, we find such differences slight.

Figure 1. Distribution of Serum 2,3,7,8-TCDD in TCP Only Workers and Referents

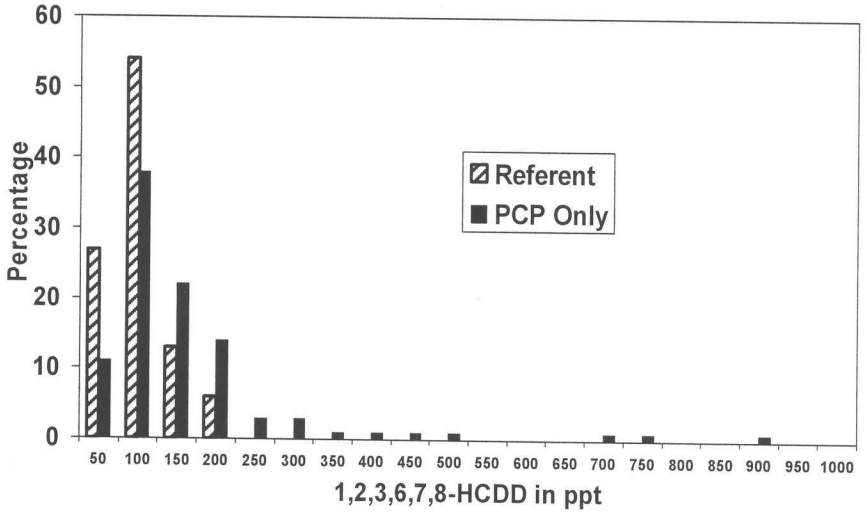


PCP workers in this study had higher levels of the hexa-, the hepta-, and the octa-chlorodioxins than the referent group. This finding is consistent with other serum studies of pentachlorophenol workers.[5, 7-9]. The level of 12378-P_5CDD is slightly higher among these workers and among workers with both TCP and PCP exposures compared to the referent group, but this difference is small. Furan contaminants have been reported in samples of commercial pentachlorophenol.[10] However, these furans have rarely been found in sera of pentachlorophenol workers.

Another group of exposed workers in our study are tradesmen. These workers had the congener profiles of both the TCP and PCP workers with high levels of 2378-TCDD and the higher chlorinated dioxins. However, tradesmen also had additional serum characteristics not seen elsewhere in our study. The first is PCB levels including PCB169 and PCB126 above the referent group. Since these tradesmen worked with equipment throughout the manufacturing site, exposure to workplace PCBs seems distinctly possible, although other workplace exposures from previous or subsequent employment cannot be ruled out. The second finding is high levels of 23478-P_5CDF and two of the hexachlorofurans, 123478-H_6CDF and 123678-H_6CDF. We see three possible explanations for this finding. Serum furans in the tradesmen could be the result of PCP exposures since furans are potential contaminants in PCP. However, we do not see this furan profile in PCP workers at this plant. Second, elevated furans could be the result of other occupational exposures at this site such as chloralkali.[11, 12] Lastly, serum furan levels may be related to exposures to PCBs. Chlorofurans are known to form as breakdown products of heating PCBs during use or the accidental failure of a capacitors and transformers.

Even though serum measurements were made many years after exposure, a sufficient number of chlorophenol workers had dioxin levels above background to enable us to examine the correlation between serum profiles and workplace exposures. Several distinct profiles distinguished TCP workers from PCP workers and other workers with no chlorophenol experience, or with more general site-wide crafts responsibilities. We find little evidence for higher pentadioxins levels in either TCP or PCP workers. The dioxin fingerprints observed in this study will be useful to future epidemiology studies that relate health effects to occupational exposures. We also note the lessons learned in constructing internal comparison groups for such investigations.

Figure 2. Distribution of Serum 1,2,3,6,7,8-HCDD in PCP Only Workers and Referents



References

1. Collins JJ, Budinsky RA, Burns CJ, et al. Serum dioxin levels in former chlorophenol workers. *J Exp Anal Environ Epi.* 2006;16:76-84.
2. Piacitelli LA, Haring Sweeney M, Fingerhut MA, et al. Serum levels of PCDDs and PCDFs among workers exposed to 2,3,7,8-TCDD contaminated chemicals. *Chemosphere.* 1992;25:251-254.
3. Ott MG, Messerer P, Zober MA. Assessment of Past Occupational Exposure to TCDD Using Blood Lipid Analyses. *Int Arch Occup Environ Health.* 1993;65(1):1-8.
4. Heederik D, Hooiveld M, Bas B-d-M. Modelling of 2,3,7,8-tetrachlorodibenzo-p-dioxin levels in a cohort of workers with exposure to phenoxy herbicides and chlorophenols. *Chemosphere.* 1998;37(9-12):1743-1745.
5. Flesch-Janys D, Becher H, Gurn P, et al. Elimination of polychlorinated dibenzo-p-dioxins and dibenzofurans in occupationally exposed persons. *J Toxicol Environ Health.* 1996;47:363-378.
6. Beck H, Eckart K, Mathar W, Wittkowski R. Levels of PCDDs and PCDFs in Adipose Tissue of Occupationally Exposed Workers. *Chemosphere.* 1989;18(1-6):507-516.
7. Papke O, Ball M, Lis A. Various PCDD/PCDF patterns in human blood resulting from different occupational exposures. *Chemosphere.* 1992;25(7-10):1101-1108.
8. Schecter AJ, Li L, Ke J, Furst P, Furst C, Papke O. Pesticides application and increased dioxin body burden in male and female agriculture workers in China. *J Occup Environ Med.* 1996;38:906-911.
9. Coenraads PJ, Olie K, Tang NJ. Blood lipid concentrations of dioxin and dibenzofurans causing chloracne. *Br J Dermatol.* 1999;141:694-697.
10. Rappe C, Gara A, Buser HR. Identification of polychlorinated dibenzofurans (PCDFs) in commercial chlorophenol formulations *Chemosphere.* 1978;21:981-991.
11. Svensson BG, Barregard L, Sallsten G, Nilsson A, Hansson M, Rappe C. Exposure to polychlorinated dioxins (PCDD) and dibenzofurans (PCDF) from graphite electrodes in a chloralkali plant. *Chemosphere.* 1993;27(1-3):259-262.
12. Hansson M, Barregard L, Sallsten G, Svensson BG, Rappe C. Polychlorinated Dibenzo-p-dioxin and Dibenzofuran Levels and Patterns in Polyvinylchloride and Chloralkali Industry Workers. *Int Arch Occup Environ Health.* 1997;70(1):51-56.