

**Serum Dioxin Levels
in Former [Dow] Chlorophenol Workers**

**Analysis and Comments
On Final Report - July, 2005**

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Introduction

In September, 2003, The Dow Chemical Company measured dioxin blood serum levels in a small number of its chlorophenol employees that were exposed to dioxins and furans present in certain pesticide plants.

The company's release of the study was a protracted, five part stage release. The staged release occurred as follows:

Chlorophenol Worker Dioxin Serum Study Release Dates

<u>Location</u>	<u>Date</u>	<u>Comments</u>
Melbourne, Australia	Oct. 2004	Oral report
Midland, MI	Nov. 2004	Press release
Lansing, MI	Dec. 2004	Oral report
Lansing, MI	Mar. 2005	Oral report slides
On-line journal	Jul. 2005	Full report

The full report is now available and further analysis and comment can be provided. A preliminary analysis of the partial data was done in May, 2005 and was available on DioxinSpin.com. This analysis supercedes the May analysis.

The full report¹ is available from the journal, the authors or on DioxinSpin.com. The study is being made available to DioxinSpin.com readers under the Fair Use Provisions of US copyright laws.

The study has value and significance to many Dow employees and residents in the Saginaw area that have been exposed to dioxins emitted by the company. A previous criticism that the study was handled more as a "PR event" rather than a high quality scientific study remains valid.

¹, Collins JJ, et al, *Serum dioxin levels in former chlorophenol workers* Journal of Exposure Analysis and Environmental Epidemiology (2005), 1-9

Analysis – Comment

The study contained a number of potential defects and shortcomings with the following being the ones of most interest.

1. *Collins, 2005* indicated that three groups of dioxin exposed workers were randomly sampled. However, a close examination of the results of the study indicates that bias may have occurred in the selection of test subjects.

Figure 1 is a chart of Serum Levels plotted versus Exposure Index expressed as a fraction of the highest reported exposure level reported as either a 2,3,7,8 TCDD exposure estimate or H/OCDD exposure estimate. As can be seen in Figure 1, 12 out of the 14 reported matched sets were at an Exposure Index of 0.25 or less. Only two data sets were at high exposure levels. Based on this correlation, It is probable that the study may have consisted of primarily low dioxin exposure employees.

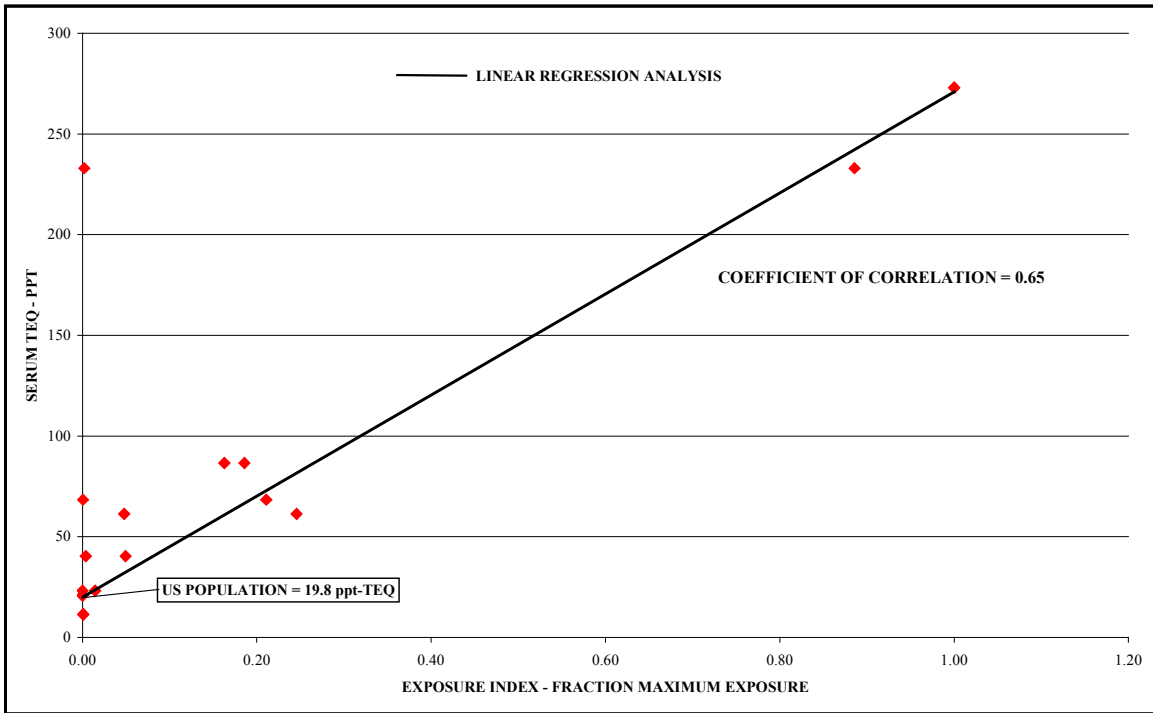
In addition, an examination of the Exposure Indices' mean values and the impact of the highest exposure level suggests that the majority of the exposure levels were below the mean and "clustered" slightly above the mean. Very few of the exposure levels reported in the study appear to be high level exposures.

Collins, 2005 did not indicate if other chlorophenol employees not included in the study had TCDD or H/OCDD exposure indices greater than the upper range reported in the study. This information would provide additional insight into the possibility that dioxin levels associated with *Collins, 2005* are at the lower range of total dioxin exposures experienced by the company's chlorophenol workers.

The reason for the apparent selection bias is not clear and it is not certain if the selection bias was coincidental or intentional. Whether the reason, if selection bias is present, the validity of the study is now in question.

A Linear Regression Analysis of the TEQ serum levels against exposure index indicates a Coefficient of Correlation of 0.65 which signifies a weak correlation between variables.

Figure 1 : TEQ Serum Levels versus Exposure Index



2. *Collins, 2005* concluded that “The exposure estimates for TCDD and the higher chlorinated dioxins... did predict current serum levels... providing validation for exposure estimates used in prior studies.”

The basis for this conclusion was not provided. There is little data in the study that supports this conclusion.

Table 1 is a summary of data presented in *Collins, 2005* on 2378-TCDD Exposure Index correlated with TCDD/PCDD dioxin levels, total TEQ levels and TEQ levels associated with TCDD/PCDD. For the purposes of this analysis, TCDD/PCDD means all tetra and penta chlorinated CDD and CDF's.

Table 1 : 2378-TCDD Exposure Index

	2378 TCDD Exposure Index (mean)	TCDD/PCDD Dioxins (1) (mean)	Total TEQ- ppt (mean)	TCDD/PCDD TEQ-ppt (2) (mean)
TCP, w/chloracne	95,572	64.8	86.8	62.1
PCP, w/chloracne	288	43.1	68.4	40.1
Chlorophenol, w/o chloracne	1971.7	30.7	40.3	28.0
Comparison employees	Not Determined	26.8	32.7	24.0

(1) All tetra, penta CDD and CDF's
(2) TEQ of all tetra, penta CDD and CDF's

As can be seen, even though TCDD exposures range from 288 to 95,572 (approximately a 330X range), the range of dioxins and TEQ's found in the study subjects is much narrower (approximately 1.5X). Dioxin serum levels of Chlorophenol employees without chloracne and Comparison Employees also without chloracne are similar.

A correlation between TCDD Exposure Index and dioxin serum levels is not apparent.

The company developed two exposure indices – one based on TCDD exposure and the other based on H/OCDD exposure. It is difficult to compare the two indices since the basis are different. The TCDD index is a 5 by 5 matrix (5 levels of TCDD “intensity” and 5 levels of “cumulative doses”. The H/OCDD index is a 4 by 4 matrix (4 levels of “intensity” and 4 levels of “cumulative doses”).

Table 2 is a summary of the information presented in *Collins, 2005* with H/OCDD exposure index correlated against H/OCDD levels, total TEQ and H/OCDD-TEQ. *Collins, 2005* referred to the previous Dow description of “H/OCDD” as “Other Dioxins”.

Table 2 : H/OCDD Exposure Index

	<u>H/OCDD (1)</u> <u>Exposure Index</u> (mean)	<u>H/OCDD</u> <u>Levels-ppt</u> (mean)	<u>Total</u> <u>TEQ- ppt</u> (mean)	<u>H/OCDD (2)</u> <u>TEQ-ppt</u> (mean)
TCP, w/chloracne	1953.8	4332.4	86.8	24.7
PCP, w/chloracne	2531.2	4064.5	68.4	28.3
Chlorophenol, w/o chloracne	592.5	1459.9	40.3	12.3
Comparison employees	Not Determined	665.4	32.7	8.7

(1) H/OCDD = *Collins, 2005* "Other Dioxins"
(2) TEQ associated with H/OCDD congeners

As can be seen, this is a mild correlation only between H/OCDD Exposure Index and TEQ resulting from H/OCDD. It is difficult to understand if this is the sole basis for the *Collins, 2005* conclusion that the study validated previous exposure level correlation's. Chlorophenol and Comparison employees without chloracne had similar TEQ serum levels.

3. *Collins, 2005* provided information on the congener levels found in the blood serums of the tested employees. An overwhelming majority of the blood serum dioxins/furans found in chlorophenol and comparison employees were the higher dioxins and furans (H/OCDD's) normally not associated with TCP and 245-T manufacture. Even at the very highest TCDD Exposure Index (514,792.6) reported in a TCP employee, H/OCDD dioxins and furans were 99.5% of the total levels found in the test subject.

Table 3 is a summary of the dioxin and furan congeners found in the study. The high percentage of H/OCDD congeners found in the blood serum of TCP workers indicates that high levels of H/OCDD exposure occurred to all study members in the past or that the Dow TCP processes were a source of large amounts of the higher chlorinated dioxins and furans, a possibility not previously reported by the company.

Table 3 : Dioxin-Furan Congener Levels – (Mean, except as indicated)

	TCDD/PCDD (1) <u>Dioxins-ppt</u>	H/OCDD (2) <u>Dioxins-ppt</u>	H/OCDD <u>% Total</u>
TCP, w/chloracne, mean	64.8	4332.4	(98.5%)
TCP, w/chloracne, maximum	266.7	47877.9	(99.5%)
PCP, w/chloracne	43.1	4064.5	(99.0%)
Chlorophenol, w/o chloracne	30.7	1459.9	(97.9%)
Tradesmen	68.5	3002.0	(97.8%)
Comparison employees	26.8	665.4	(96.1%)
(1) All tetra, penta CDD and CDF's			
(2) All other dioxins			

4. *Collins, 2005* reported that 1,378 of the original cohort of dioxin-exposed pesticide workers were still alive as of December 31, 2002. In order to achieve a 95% ± 5% Confidence Level that dioxin blood serum levels are accurately known, a sample size of 301 employees is required. However, only 62 chlorophenol employees were tested. The company did not report the confidence level associated with the very small sampling of workers.

Collins, 2005 indicated that the sampled employees were selected randomly but provided no information as to whether employees with severe illnesses, such as cancers linked to dioxin exposure, were included in the sampling or were excluded. Sampling of only healthy workers may have introduced substantial bias into the study.

5. The study included 36 non-chlorophenol workers that were exposed to dioxins present in the ambient environment of the Midland plant. The comparison group was matched on birth date and hire date to the chlorophenol workers to produce similar age and year of hire distributions between groups.

It is believed that general dioxin levels peaked in the late 1960's and early 1970's with dioxin exposures being potentially higher in outdoor work environments than in office locations for all years in which dioxins were produced and emitted.

The study did not provide any information as to where the 36 "non-exposed" employees worked in the Midland plant and the types of jobs associated with the comparison group.

Table 4 provides a comparison of dioxin serum levels between the Dow comparison group and US background (adjusted) presented in *Patterson, 2004*². On average, the Dow comparison employees (63, 86 years of age) were found to have a higher level of serum dioxins than did similar age groups of the US population. The Oldest employees in the comparison group exhibited an even greater level of serum dioxins than did the equivalent age group in the US population.

Table 4 : Dioxin Serum Levels – Dow Comparison Employees

	Dow Comparison Employees	US Population (1)
Age, years	63 (47 - 86)	63 (47 - 86)
Serum TEQ, ppt	** 32.7 (10.7 - 96.7)	19.8 (12.7-29.7) (2)
Serum TEQ, ppt		
47 yrs. of age	10.7 (NR)	12.0 (2.1 - 33.2)
63 yrs of age	** 32.7 (NR)	19.8 (1.4 - 32.5)
86 yrs of age	** 96.7 (NR)	29.7 (12.0 - 42.4)
(1) <i>Patterson, 2004</i> adjusted		
(2) <i>Patterson, 2004</i> linear regression values		
**Exceeds US background levels		

Reference range data from *Patterson, 2004* was adjusted to exclude four (4) out of the 588 subjects that were found to have unexplained abnormally high serum levels. In addition, *Patterson, 2004* background levels (1996, 1997, 2001) were recalculated to

² Patterson DG, et al, *Age Specific Dioxin TEQ Reference Range*, Organohalogen Compounds, Vol 66 (2004)

2004 levels. More information on the basis for the adjustments can be found in DioxinSpin.com/Flawed Science/Volume 4.

6. *Collins, 2005* provided dioxin serum level information on four (4) groups of chlorophenol workers exposed to a wide range of TCDD and H/OCDD exposures. All four groups were found to have not only higher mean levels but also higher upper ranges of serum dioxins than the background US population. The mean average for all four groups was approximately 3.5 times the US background mean. The upper ranges found in the chlorophenol workers were approximately 6.4 times the upper end of the range in the US population. Table 5 is a summary of the overall dioxin blood serums found in the Dow study.

Table 5 : Dioxin Serum Levels – Chlorophenol Workers

	TEQ - ppt	
	<u>Mean</u>	<u>Range</u>
TCP w/chloracne	86.8**	11.4 - 273.0**
Tradesmen	85.0**	16.0** - 193.0**
PCP w/chloracne	68.4**	23.2** - 233.3**
Chlorophenol w/o chloracne	40.3**	20.8** - 61.3**
Dow comparison employees	32.7**	10.7 - 96.7**
US background population (1)	19.8	12.7 - 29.7

(1) *Patterson, 2004* adjusted
 ** Exceeds US population levels

7. *Collins, 2005* suggests that dioxin exposures incurred while working in other departments contributed to the serum levels being found in the tradesmen. “We did observe some participants [tradesmen] with high serum dioxin and furan levels who worked in nonchlorophenol departments.” It is well recognized that employees that worked in Waste Control Operations (close proximity to the chemical waste incinerators,

tar burners and chemical ponds) and Chlorobenzene workers have a significant potential for high dioxin exposure. If the company is aware of other departments other than chlorophenol, waste control and chlorobenzene that contributed to dioxin serum levels, this information has been kept confidential. The study did not provide any additional information on this matter.

Further explanation of the work history and management of the “tradesworkers” is appropriate since *Collins, 2005* may have created more confusion than clarity.

The study is correct in stating that these tradesmen were not assigned to the Chlorophenol Department. The tradesmen were actually part of the Maintenance Department. However, it was a common practice to have Maintenance Service Units assigned primarily to one production department. Although the maintenance personnel were “loaned out” for brief periods of time to assist in maintenance “turnarounds” in other plants, the majority of the time would still be spent in the assigned production department – in this case, Chlorophenol Production. In a number of Dow mortality studies of chlorophenol workers, the chlorophenol maintenance workers were included in the cohort of dioxin exposed workers. The chlorophenol “tradesmen” numbered approximately 475 workers – 21% of the total 2000 of dioxin exposed workers.

The use of the term “plant wide duties” is correct. However, unless the chlorophenol tradesmen worked for an extended period of time in Waste Control operations or the Chlorobenzene plants, the majority of the tradesmen dioxin exposure would have occurred while working in the chlorophenol production plants.

Based on the information contained in *Bond, 1989*³, the chlorophenol tradesmen were included in the various dioxin exposure indices reported by the company in this and other studies.

It is understandable that the company could not provide a dioxin exposure index for the plant-wide comparison employees. It is somewhat surprising that *Collins, 2005* did not

³ Bond GG, et al, *Incidence of Chloracne among Chemical Workers Potentially Exposed to Chlorinated Dioxins*, Jour of Occup Med, Vol 31 No 9 (September, 1989)

provide any information of the dioxin exposure levels of the chlorophenol tradesmen. Based on *Bond, 1989*, the information should be available.

8. *Collins, 2005* provided information on the levels of TCDD that potentially could have been present in study employees when acute dioxin exposure was discontinued approximately 24 to 63 years ago. However, the information was not presented in a table and the significance of the information may not have been totally understood by the readers of *Collins*.

Table 6 is a summary of the information provided on dioxin serum levels in earlier years.

Table 6 : Dioxin Serum Levels - Last Workplace Exposure (24 to 63 years prior)

	TCDD Levels Mean (range) ppt	TEQ Levels Mean (range) ppt
Current Levels, 2003	16.7 (2 - 176)	68.4 (11.4 - 273)
Half-life model, 9 yrs.	267 (4 - 1,212)	3,990 (nr - 17,616)(a)
Half-life model, 7 yrs.	582 (9 - 2,641)	8,700 (nr - 38,400)
Toxicokinetic model	1928 (22 - 17,847)	nr
nr = Not Reported		
(a) Estimated		

It is recognized that not all persons with high levels of TCDD or TEQ in their blood serum develop cancer. However, TCDD is a known human carcinogen. Several high quality mortality studies have correlated TCDD blood serum levels of 233 ppt to 462 ppt with a 15% to 410% increase in the expected mortality from cancer. Although current TCDD levels found in *Collins, 2005* were below this level, serum levels in prior years were at these levels and higher.

9. *Collins, 2005* provided some background information on TCDD serum levels found in other studies. However, dioxin levels were determined in multiple years and a comparison to the Dow findings is difficult. Adjusting all serum levels to a common year

allows for an easier comparison. In addition, the Dow study did not provide information concerning increases in overall cancer mortality even though this type of information was available in some of the cited studies.

Table 7 : TCDD Blood Serum Levels Found in Other Studies (adjusted to 1990 levels)

Population	TCDD Serum Level (Range - ppt)	Increase in All Cancers - %
NIOSH Registry	2 - 3,389	46%
Midland, USA - Collins	9 - 777	nr
Ludwigshafen, GE (BASF)	1 - 744	100% (a)
Austria	98 - 659	
Times Beach, MO	5 - 577	
Hamburg, GE (Boehringer)	27 - 543	30% - 70%
Ranch Hand, USAF	6 - 381	
Seveso, Italy (mean)	12 - 112	30% (b)
New Plymouth, NZ, IWD (c)	nr	69%

nr = Not Reported
(a) >20 yrs latency, with chloracne
(b) TCDD only, acute exposure only
(c) Dow Joint Venture - TCP, 245-T production

It is believed that the NIOSH Registry data base on TCDD serum levels does not include any information on Dow Chemical employees. On the assumption that Dow's TCDD exposure levels were similar to those found in other plants in the NIOSH registry, the upper range of the Dow TCDD serum levels (777 ppt) is substantially below the upper range reported by NIOSH (3,389 ppt). This supports the contention that the chlorophenol workers studied in *Collins, 2005* may be at the lower end of the TCDD exposure spectrum.

10. *Collins, 2005* found an increase of TCDD serum levels of 2.2 ppt for every 10 years of age in the chlorophenol cohort. This rate of serum level increase is low in comparison to the rate found by the New Zealand Ministry of Health in its study of New Plymouth, NZ residents exposed to dioxin emissions from the Ivon-Watkins Dow TCP/245-T plant. The IWD plant was a Dow Chemical joint venture and utilized the most recent TCP process employed at the Midland plant to produce 245-TCP. The IWD site is now a part of the Dow AgriSciences.

Collins, 2005 did not discuss TCDD bio-accumulation rates in any other study. Based on the higher levels of TCDD known to be present in the Midland plant, it is surprising that TCDD serum levels in chlorophenol employees increased at the low rates that were reported.

Table 8 provides information of the differences in TCDD bio-accumulation rates between chlorophenol employees, New Plymouth residents and the average US population.

Table 8 : TCDD Bio-Accumulation

Population	TCDD Blood Serum PPT per 10 Years	TCDD (ppt) Soil Levels
New Plymouth, NZ (a)	4 - 5	12 (1997)
Midland, USA	2.2	145 (1986) 25 (1996)
US Background (b)	0.4	2 - 5 (1983) < 2 (1996)

(a) New Zealand Ministry of Health, 2005
(b) CDC, *Patterson 2004*

Conclusions of Analysis

A. The study does provide some sorely needed information on dioxin levels in the blood serum levels of some of The Dow Chemical Company's most highly exposed chemical workers. However, there is information that suggests that the study primarily consisted of employees with low dioxin exposures. If this observation is correct, the intent of the company in producing such a limited study is not clear.

B. The study confirms that Comparison Employees that worked in the Midland plant at jobs not associated with production plants producing dioxins and furans have dioxin blood serum levels significantly greater than the same age group in the US population.

Dioxin serum levels in the sampled chlorophenol employees were found to be significantly higher than the background levels found in the US population.

C. Dioxin blood serum levels found in the tested employees consist primarily (>96%) of H/OCDD dioxins and furans. Even an employee with the highest level of TCDD (266.7 ppt) had an extremely high level of H/OCDD dioxins/furans (47,877.9 ppt) to the extent that H/OCDD dioxins represented 99.5% of the total dioxins and furans found in the subject's blood serum.

D. TCDD serum levels found in the study cohort are in the range in which other studies cited by *Collins, 2005* reported a significant increase in All Cancers. *Collins, 2005* did not provide any updated mortality information on its approximately 2,200 employees exposed to high levels of dioxins and furans.

E. The study was based on 62 chlorophenol workers and tradesmen. To achieve a 95 ± 5% confidence level that dioxin serum levels in the still living members (1,378) of the original cohort are accurately known, a sample size of 301 employees would be required. The study did not provide any guidance on the confidence level and interval associated with the smaller sampling.

F. The study failed to adjust background age group dioxin serum levels found in the US population in 1996, 1997 and 2001 to the year of the chlorophenol employee sampling :

2003. When this adjustment is made (plus exclusion of four abnormally high serum levels), both Comparison and Chlorophenol employees were found to have significantly higher levels of dioxin in the blood serum than US population background age groups.

G. The TCDD bio-accumulation rate (ppt increase per 10 years) found in the chlorophenol workers was approximately 50% of the rate found in persons residing in close proximity to a Dow 245-TCP/245-T manufacturing facility in New Plymouth, New Zealand. Based on the much higher degree of TCDD exposure to the chlorophenol workers, the employees lower bio-accumulation rate is unusual.

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