Appendix H

1. IMPLICATIONS OF STATISTICAL ASSESSMENT OF NEW ZEALAND SURVEYS OF DIOXINS IN BLOOD FOR DETECTION OF "EXCESS" LEVELS OF 2,3,7,8-TCDD IN PEOPLE POTENTIALLY EXPOSED TO EMISSIONS FROM THE DOW 245-T PLANT.

One of the key purposes of the proposed sampling of blood from people potentially exposed to 2,3,7,8-TCDD as a result of living in the vicinity of the Dow 245-T plant is to determine whether their blood levels of 2,3,7,8-TCDD are significantly higher than those of the typical New Zealand population, and whether any such "excess" level of 2,3,7,8-TCDD indicates the possibility of past exposures that may have produced adverse health effects. Accordingly, a means of distinguishing between high 2,3,7,8-TCDD levels in blood that may simply result from the variation between individuals within the typical population and those concentrations that are too high to be accounted for by variation within the typical population is required.

Two methods have been considered as possible means of making these distinctions:

1. Estimation of the variation in the typical New Zealand population, as characterised by the standard deviation in the 2,3,7,8-TCDD levels for particular age groups of each sex;
2. Estimation of the expected "typical" 2,3,7,8-TCDD level for any individual, based on the ratio of 2,3,7,8-TCDD to other dioxin and furan congeners in the typical New Zealand population, and the concentrations of those congeners in the individual's blood.

Two sets of data on the levels of dioxins and furans in the blood of New Zealanders are available:

- A survey of 28 individuals, reported by Hannah et al (1994);
- A survey using pooled blood samples collected from about 1800 individuals pooled into 80 samples for analysis (the MfE survey, Buckland et al. (2001)).

The ideal set of data for the purpose of defining the range of 2,3,7,8-TCDD levels in the typical New Zealand population, or for defining appropriate ratios between congeners and the variability in those ratios in the typical population, would consist of data for a large number of individuals, without pooling. Neither of the available sets is ideal. The Hannah data set is too small, particularly when it is noted that 2,3,7,8-TCDD levels were below the detection limit for 7 of the individuals, effectively reducing the data set to 21 individuals. The pooling of samples in the MfE survey reduces the certainty of estimation of the level of variation in the typical population and also makes the data unsuitable for assessment of the possible use of congener ratios for estimating expected individual 2,3,7,8-TCDD levels.

1.1 COMPARISON OF THE HANNAH AND MFE DATA SETS.

Standard deviations for the various age ranges for both males and females were estimated for the MfE data set from the standard deviation for the pooled sets of data for each age range and gender, as described in the Appendix. No distinction has been made between ethnicity (Maori and Non-Maori) when analyzing the pooled MfE blood samples. Standard deviations for the Hannah data were calculated directly from the individual results.

The mean 2,3,7,8-TCDD concentrations, the standard deviations and coefficients of variation (relative standard deviation) from both the Hannah and MfE data sets are presented in Table 1. The age ranges for the two surveys are not the same, but the data have been arranged according to increasing mid-point age for the ranges.

Table 1. Comparison of the Hannah et al. (1994) and MfE data for 2,3,7,8-TCDD in blood lipid

	Age range	Survey	Mean	Pooled sample standard deviation	Pooled sample coefficient of variation	Estimated population standard deviation	Estimated population coefficient of variation	Pools	Individuals
			ng/kg lipid			ng/kg lipid			
Female	15-24	MfE	1.1	0.09	9%	0.42	39%	7	143
Female	20-29	Hannah	1.8			0.45	25%		3
Female	25-34	MfE	1.5	0.27	18%	1.39	90%	11	283
Female	30-39	Hannah	2.2			0.70	31%		4
Female	35-49	MfE	2.1	0.41	19%	1.90	89%	12	265
Female	40-60	Hannah	3.8			1.54	41%		5
Female	50-64	MfE	3.6	1.0	27%	4.70	132%	7	165
Female	64+	MfE	5.9	1.00	17%	5.09	86%	6	155
Male	15-24	MfE	1.0	0.24	25%	1.13	117%	5	112
Male	20-29	Hannah	1.3			0.07	6%		2
Male	25-34	MfE	1.2	0.26	21%	1.17	94%	8	162
Male	30-39	Hannah	1.8			0.43	25%		4
Male	35-49	MfE	1.8	0.34	19%	1.61	91%	10	228
Male	40-60	Hannah	2.1			1.05	50%		3
Male	50-64	MfE	2.5	0.27	11%	1.23	49%	7	150
Male	64+	MfE	3.0	0.29	9%	1.44	48%	5	126

The mean 2,3,7,8-TCDD concentrations and their variation between the different age groups are similar in both surveys.

The standard deviations calculated for the Hannah data are either similar to or, in most cases, smaller than the estimated population standard deviations for the MfE survey. However, there is a relatively high level of uncertainty about the accuracy of the standard deviations calculated from the Hannah data, because of the small number of samples in each population and gender group. The estimated population standard deviations for females from the MfE survey increase markedly with age, while those for males are either approximately constant or increase slightly with increasing age.

Ideally, the standard deviations for the Hannah data would better be calculated using expressions that take into account the small number of data points. However, it appears very likely that the Hannah survey reflects only a segment of the New Zealand population, rather than the full variability reflected better in the MfE survey. This possible representation of only a segment of the total New Zealand population in the Hannah data is a potential limitation on the use of this data as a basis for the congener ratio method in bullet point 2 above.

1.2 IDENTIFICATION OF "EXCESS" 2,3,7,8-TCDD BASED ON TYPICAL POPULATION MEANS AND STANDARD DEVIATIONS.

Table 2 sets out the means and standard deviations of 2,3,7,8-TCDD concentrations in blood lipids for the two New Zealand surveys, together with the 2,3,7,8-TCDD concentrations corresponding to 1.65, 2 and 3 standard deviations and the total concentrations 1.65, 2 and 3 standard deviations above the mean concentrations. The 1.65 standard deviations figure corresponds to the 95%ile. A concentration higher than 2 standard deviations above the mean would occur only in 2.3% of the population. The corresponding percentage of the population with concentrations higher than 3 standard deviations above the mean is 0.14%. Depending on the level of certainty desirable in identification of "excess" 2,3,7,8-TCDD, any of these total concentrations could be chosen as the concentrations above which at least some "excess" 2,3,7,8-TCDD above that expected for the typical population could be considered to be present in any particular sample from a person who has potentially been exposed to emissions from the Dow plant.

Table 2. Estimation of 2,3,7,8-TCDD concentrations above which "excess" 2,3,7,8-TCDD can be considered to be present.

	Age range	Survey	Mean	Estimated population standard deviation	Increases for			Total concentrations for		
					95%ile	2 SD	3 SD	95%ile	2 SD	3 SD
			ng/kg lipid							
Female	15-24	MfE	1.1	0.4	0.7	0.8	1.3	1.8	1.9	2.4
Female	20-29	Hannah	1.8	0.5	0.7	0.9	1.4	2.6	2.7	3.2
Female	25-34	MfE	1.5	1.4	2.3	2.8	4.2	3.8	4.3	5.7
Female	30-39	Hannah	2.2	0.7	1.2	1.4	2.1	3.4	3.6	4.3
Female	35-49	MfE	2.1	1.9	3.1	3.8	5.7	5.3	5.9	7.8
Female	40-60	Hannah	3.8	1.5	2.5	3.1	4.6	6.3	6.9	8.4
Female	50-64	MfE	3.6	4.7	7.8	9.4	14.1	11.3	13.0	17.7
Female	64+	MfE	5.9	5.1	8.4	10.2	15.3	14.3	16.1	21.2
Male	15-24	MfE	1.0	1.1	1.9	2.3	3.4	2.8	3.2	4.3
Male	20-29	Hannah	1.3	0.07	0.1	0.1	0.2	1.4	1.4	1.5
Male	25-34	MfE	1.2	1.2	1.9	2.3	3.5	3.2	3.6	4.7
Male	30-39	Hannah	1.8	0.4	0.7	0.9	1.3	2.5	2.6	3.1
Male	35-49	MfE	1.8	1.6	2.7	3.2	4.8	4.4	5.0	6.6
Male	40-60	Hannah	2.1	1.1	1.7	2.1	3.2	3.8	4.2	5.3
Male	50-64	MfE	2.5	1.2	2.0	2.5	3.7	4.6	5.0	6.2
Male	64+	MfE	3.0	1.4	2.4	2.9	4.3	5.4	5.9	7.3

Orloff et al., (2001) report data from a survey of dioxin and furan concentrations in blood samples from a population potentially exposed to industrial emissions, compared with the typical American population, in which they use the 95 percentile concentrations for each age as the criterion for elevated levels possibly attributable to industrial emission exposures.

The ratio of the 95 percentile concentration to the mean concentration for the general population group from the Orloff et al. paper provides a useful cross-check on the variability estimated from the MfE data. The 95%ile/mean ratio from the Orloff paper is 2.1, compared with an average of 2.4 over the various age and gender groups from the MfE data, with a range of 1.6-3.2. Accordingly, the population variability for the concentrations of 2,3,7,8-TCDD appear similar between the MfE data and that used by Orloff et al.

People who are in the age range 50-64 in 2003 are likely to be those of most interest, since these people would have been, for example, aged 15-29 in 1968. For this age range, women would need to have 2,3,7,8-TCDD concentrations in blood lipids above 11.3 ng/kg (95%ile) 13 ng/kg (2 SD) or 17.7 ng/kg (3 SD) for a moderate to high probability that at least some of the 2,3,7,8-TCDD in their blood could not be accounted for by the range of concentrations in the typical New Zealand population. The equivalent concentrations for men are 4.6ng/kg 5.0 ng/kg (2 SD) and 6.2 (3 SD).

Some further adjustments may be necessary to account for possible decreases in general population 2,3,7,8-TCDD concentrations between the date of the MfE samples (December 1996-November 1997) and 2003. However, any such adjustments will be minor compared with the typical population variability indicated by the survey data.

Both the mean 2,3,7,8-TCDD concentrations and the estimated standard deviations for men are notably smaller than those for women. Further, for the 50-64 age group, the ratio of the

residual 2,3,7,8-TCDD in 2000 resulting from any particular level of exposure over the period 1962-1972 to the estimated standard deviation of typical population 2,3,7,8-TCDD concentrations in the MfE survey for men is double that for women. Accordingly, there is evidently a greater likelihood of demonstrating the presence of "excess" 2,3,7,8-TCDD from past exposures to emissions from the Dow plant for men of this age group than for women. However, the indicated substantially higher concentrations of 2,3,7,8-TCDD in women than in men mean that the concentrations in both men and women will be of interest.

On the other hand, the ratio of the residual 2,3,7,8-TCDD in 2000 resulting from any particular level of exposure over the period 1962-1972 to the estimated standard deviation of typical population 2,3,7,8-TCDD concentrations in the MfE survey for men in the 35-49 age group is 0.6 times that for women.

Accordingly, it is not clear whether the apparently greater "detectability" of "excess" 2,3,7,8-TCDD resulting from exposure to emissions from the Dow plant for women in the 50-64 age group is just an artefact of the uncertainties in the estimation of the typical population standard deviations and the modelled residual concentrations resulting from any particular 2,3,7,8-TCDD exposure.

The higher concentrations found in women particularly in the older age group is consistent with the longer half-life for 2,3,7,8-TCDD used in the toxicokinetic model.

1.3 CONGENER RATIO METHOD.

If the ratio of 2,3,7,8-TCDD to another congener were constant in the typical population, the "typical population" level of 2,3,7,8-TCDD could be calculated for a sample from a person potentially exposed to emissions from the Dow plant as follows:

$$[2,3,7,8\text{-TCDD}]_{\text{typical population}} = [\text{congener}] \times (\text{congener ratio})$$

where

$[2,3,7,8\text{-TCDD}]_{\text{typical population}}$ is the "typical population" concentration of 2,3,7,8-TCDD expected in the sample from the potentially exposed person

[congener] is the concentration of the congener in the sample from the potentially exposed person

(congener ratio) is the ratio of 2,3,7,8-TCDD to the congener in the typical population

However, the ratios between the concentrations of 2,3,7,8-TCDD and the other dioxin congeners are not constant in the typical population and whether this method will be useful depends on the level of variability in these ratios.

Table 3 gives data about the ratios of 2,3,7,8-TCDD took other congeners from both the Hannah and MfE surveys. The availability column indicates the percentage of samples from the Hannah survey for which the concentration of the particular congener was above the detection limit in samples for which the concentrations of 2,3,7,8-TCDD was above the detection limit. A high availability is obviously desirable. The 2,3,7,8-TCDD concentrations were below the detection limit in serum samples taken from 7 of the 28 participants in the study.

Table 3. Congener ratio data

	Availability	Coefficient of variation	Max/Min	Hannah ratio	MfE ratio	Hannah /MfE
2,3,7,8 TCDF	14%	52%	3.4	4.1	9.9	0.42
2,3,7,8 TCDD	100%					
1,2,3,7,8 PeCDF	0%				13.1	
2,3,4,7,8 PeCDF	95%	33%	3.7	0.73	0.55	1.32
1,2,3,7,8 PeCDD	90%	36%	3.6	0.54	0.48	1.15
1,2,3,4,7,8 HxCDF	71%	39%	6.3	0.88	1.02	0.86
1,2 ,3 ,6,7,8 HxCDF	76%	34%	3.7	0.89	0.86	1.03
2,3,4,6,7,8 HxCDF	24%	48%	4.1	2.8	2.90	0.98
1,2,3,7,8,9 HxCDF	0%					
1,2,3,4,7,8 HxCDD	90%	42%	8.8	0.86	0.80	1.07
1,2,3,6,7,8 HxCDD	95%	38%	4.2	0.09	0.11	0.83
1,2,3,7,8,9 HxCDD	100%	42%	4.8	0.47	0.53	0.89
1,2,3,4,6,7,8 HpCDF	100%	55%	8.1	0.34	0.48	0.70
1,2,3,4,7,8,9 HpCDF	0%				7.1	
1,2,3,4,6,7,8 HpCDD	100%	40%	5.7	0.032	0.058	0.56
OCDF	0%					
OCDD	100%	52%	5.5	0.0039	0.0062	0.63

The coefficient of variation and max/min columns indicate the variability in the ratios for the Hannah survey. The coefficients of variation are calculated as the standard deviation for all 21 samples in this study for which the 2,3,7,8-TCDD concentrations were above the detection limit. Comparison of the Hannah and MfE ratios indicate the degree to which these ratios are consistent between these two sets of data.

Of the congeners showing 90% or more availability, the ratios for 1,2,3,4,6,7,8 HpCDD and OCDD differ markedly between the Hannah and MfE surveys. The Hannah survey concentrations of both 1,2,3,4,6,7,8 HpCDD and OCDD are about double those of the MfE survey. To a slightly smaller degree, there is also a substantial difference between the ratios for 1,2,3,4,6,7,8 HpCDF between the Hannah and MfE surveys. These three congeners are not considered suitable for use in the congener ratio method because of the lack of consistency between the two sets of survey data.

Of the other congeners for which the availability is 90% or above, all have ratios to 2,3,7,8-TCDD with coefficients of variation in a range 33-42%. 2,3,4,7,8 PeCDF has the largest discrepancy between the Hannah and MfE ratios, and if this congener is omitted from consideration, the range of coefficients of variation is 36-42%. Of the remaining congeners, 1,2,3,7,8,9 HxCDD has the highest availability, and is assessed further here.

The coefficients of variation for ratios of 2,3,7,8-TCDD to 1,2,3,7,8,9 HxCDD for the typical population were estimated from the 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD ratios for the sample pools by the same method used to estimate the typical population coefficients of variation for 2,3,7,8-TCDD concentrations. This approach can only provide an approximate estimate of the standard deviation of ratio as intended for indicative purposes. Table 4 compares the coefficients of variation estimated for these ratios with the estimated coefficients of variation

for 2,3,7,8-TCDD concentrations. The table also includes the coefficients of variation for the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD for the various gender and age groups from the Hannah study.

Table 4. Comparison of variability in 2,3,7,8-TCDD concentrations and ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD in NZ surveys

MfE Survey	Age group	Estimated population coefficient of variation of 2,3,7,8 TCDD concentration	Estimated population coefficient of variation of ratio of 2,3,7,8 TCDD to 1,2,3,7,8,9 HxCDD
F	15-24	39%	62%
F	25-34	90%	72%
F	35-49	89%	75%
F	50-64	132%	107%
F	64+	86%	92%
M	15-24	117%	147%
M	25-34	94%	69%
M	35-49	91%	72%
M	50-64	49%	53%
M	64+	48%	41%
Averages		83%	79%
Hannah Survey			
F	20-29	25%	62%
F	30-39	31%	8%
F	40-60	41%	41%
M	20-29	6%	31%
M	30-39	25%	27%
M	40-60	50%	13%
Averages		30%	30%
Ratios MfE/Hannah		2.8	2.6

The ranges of coefficients of variation for 2,3,7,8-TCDD concentrations and for the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD are similar in each of the MfE and Hannah surveys, and the difference in ranges between the two surveys is also similar for the 2,3,7,8-TCDD concentrations and for the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD. The average of the coefficients of variation is also closely similar for both 2,3,7,8-TCDD concentrations and for the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD in each of the MfE and Hannah surveys. The increase in the average of the coefficient of variation between the MfE and Hanna surveys is also closely similar.

In the absence of this information, it could be considered possible that use of the pooled sample data from the MfE survey might underestimate the variability in the general population of the ratio between congeners, because of the possibility that the pooling of samples from individuals might balance out the ratios for individuals with very high and very low ratios included in the pool. The similarity in the variability for both 2,3,7,8-TCDD concentrations and the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD demonstrated in Table four strongly suggests that such possible balancing out effects are not significant, and that

reasonable estimates of the general population variability in the congener ratios are likely to be obtained from the pooled samples data, as done here.

As for the 2,3,7,8-TCDD concentrations, the variability for the 2,3,7,8-TCDD/X ratio estimated from the MfE survey is substantially greater than for the Hannah data. Accordingly, it is more appropriate to use the MfE data.

Table 5 sets out data for the ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD.

Table 5. Ratios of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD from the MfE survey

Sex	Age range	Weighted mean ratios	Estimated Population SD	Estimated Population CV	Mean ratio +2SD	Mean ratio +3SD
F	15-24	0.36	0.23	62%	0.8	1.0
F	25-34	0.42	0.30	72%	1.0	1.3
F	35-49	0.50	0.38	75%	1.3	1.6
F	50-64	0.66	0.71	107%	2.1	2.8
F	64+	0.83	0.77	92%	2.4	3.1
M	15-24	0.39	0.57	147%	1.5	2.1
M	25-34	0.47	0.32	69%	1.1	1.4
M	35-49	0.48	0.34	72%	1.2	1.5
M	50-64	0.59	0.31	53%	1.2	1.5
M	64+	0.63	0.26	41%	1.1	1.4

Table 6 applies the congener method based on the ratio of 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD to the data for individual samples from the Hannah study .

For a normally-distributed population, 2.3% of the population would lie above the mean plus 2 standard deviations and 0.14% of the population would lie above the mean plus 3 standard deviations. Accordingly, it is very unlikely that "typical population" concentrations of 2,3,7,8-TCDD would be higher than those calculated for 2 standard deviations, and more particularly those for 3 standard deviations, above the mean estimates in Table 6.

In the majority of cases, the maximum "typical population" 2,3,7,8-TCDD concentration estimated from the 2,3,7,8-TCDD concentrations of the MfE survey gives the lower maximum, and is therefore the more highly discriminatory criterion to determine when "excess" 2,3,7,8-TCDD is present in the blood from any individual potentially exposed to emissions from the Dow plant. However, the congener method based on 1,2,3,7,8,9 HxCDD may provide useful confirmation of the assessments based on 2,3,7,8-TCDD concentrations only, and in some instances is likely to allow identification of "excess" 2,3,7,8-TCDD concentrations at lower levels than the 2,3,7,8-TCDD concentration method.

Table 6. Application of the 2,3,7,8-TCDD/1,2,3,7,8,9 HxCDD congener ratio method and 2,3,7,8-TCDD concentration methods for typical population maximum 2,3,7,8-TCDD concentrations using the Hannah study data

Age and gender group	Hannah study data		Mean ratio	Max "typical" 2,3,7,8 TCDD at +2SD from		Mean ratio	Max "typical" 2,3,7,8 TCDD at +3SD from	
	1,2,3,7,8,9 HxCDD	2,3,7,8 TCDD	+2SD	ratios	concentrations	+3SD	ratios	concentrations
	ng/kg lipid			ng/kg lipid			ng/kg lipid	
40-60 F	4.7	3.1	2.1	9.9	10.2	2.8	13.2	14
40-60 F	8.3	3.8	2.1	17.4	10.2	2.8	23.2	14
40-60 F	4.2	1.7	2.1	8.8	10.2	2.8	11.8	14
40-60 F	6.6	4.6	2.1	13.9	10.2	2.8	18.5	14
40-60 F	5.3	5.8	2.1	11.1	10.2	2.8	14.8	14
40-60 M	7.8	3.2	1.2	9.4	4.8	1.5	11.7	6.3
40-60 M	3.4	1.1	1.2	4.1	4.8	1.5	5.1	6.3
40-60 M	2.6	<1	1.2	3.1	4.8	1.5	3.9	6.3
40-60 M	4.2	<2	1.2	5.0	4.8	1.5	6.3	6.3
40-60 M	4.9	2.0	1.2	5.9	4.8	1.5	7.4	6.3
30-39 F	3	1.4	1.3	3.9	6.0	1.6	4.8	8.0
30-39 F	6.9	2.7	1.3	9.0	6.0	1.6	11.0	8.0
30-39 F	6.8	2.9	1.3	8.8	6.0	1.6	10.9	8.0
30-39 F	4.7	1.9	1.3	6.1	6.0	1.6	7.5	8.0
30-39 F	8.3	<3	1.3	10.8	6.0	1.6	13.3	8.0
30-39 M	6.3	1.7	1.2	7.6	4.2	1.5	9.5	5.3
30-39 M	5.8	1.6	1.2	7.0	4.2	1.5	8.7	5.3
30-39 M	3	1.4	1.2	3.6	4.2	1.5	4.5	5.3
30-39 M	6.1	2.4	1.2	7.3	4.2	1.5	9.2	5.3
30-39 M	7.1	<3	1.2	8.5	4.2	1.5	10.7	5.3
20-29 F	2.4	1.8	1.0	2.4	2.8	1.3	3.1	3.5
20-29 F	6.6	2.3	1.0	6.6	2.8	1.3	8.6	3.5
20-29 F	6.2	1.4	1.0	6.2	2.8	1.3	8.1	3.5
20-29 F	3.9	<1	1.0	3.9	2.8	1.3	5.1	3.5
20-29 M	2	1.3	1.5	3.0	3.6	2.1	4.2	4.8
20-29 M	7.7	<4	1.5	11.6	3.6	2.1	16.2	4.8
20-29 M	2.9	1.2	1.5	4.4	3.6	2.1	6.1	4.8
20-29 M	2.3	<1	1.5	3.5	3.6	2.1	4.8	4.8

It is also possible that the congener ratio method based on other congeners in Table 3 with high availability and mean ratios similar between both the Hannah and MfE survey data may provide additional confirmation or discrimination. The best congener ratio approach will probably be to use all congeners unless there is clear evidence that the particular congener ratio is unsuitable or unreliable

It is possible that the ratios between 2,3,7,8-TCDD and some of the other congeners may be similar to those for emissions from the Dow plant during the period of particular interest (probably 1962-1975). For example, the trichlorophenol used for production of 245-T might contain both 1,2,3,6,7,8 HxCDD and 1,2,3,7,8,9 HxCDD in addition to 2,3,7,8-TCDD, via formation from tetrachlorophenol. If this is the situation, the congener ratio method would not give a useful indication of maximum "typical population" concentrations of 2,3,7,8-TCDD in samples from individuals potentially exposed to Dow plant emissions. However, if the congener ratio method indicates a substantially lower maximum "typical population"

concentration of 2,3,7,8-TCDD than the measured level of 2,3,7,8-TCDD in the sample, this will be a reliable indication of the presence of "excess" 2,3,7,8-TCDD.

It is also possible that, if the congener ratio for a particular congener is not distinguishably different from that of the typical population, but the 2,3,7,8-TCDD concentration is clearly higher than for the typical population, the individual might have been exposed to unusually high intakes from the same sources applicable to the general population, rather than to emissions from the Dow plant. This might happen, for example, as a result of unusual dietary habits.

1.4 MULTI-COMPONENT ANALYSIS.

Orloff et al. used multi-component analysis in evaluation of their data. This showed a marked difference in the congener composition between those samples falling within the 95 percentile concentrations for the general population estimated for the different ages compared with those exceeding the 95 percentiles, most of which were from the population tested in relation to possible exposure to industrial emissions.

This technique is very likely to be useful in the study of exposures associated with the Dow plant.

1.5 MULTIPLE REGRESSION ANALYSIS.

Orloff et al. used this technique to examine whether period of residence in the area potentially subject to industrial exposures contributed to higher levels of dioxins in blood. This showed that if increasing dioxin concentrations associated with increases in age were controlled for, there was no demonstrable increase associated with increasing periods of residence. This may well not be the situation in the Paritutu area, and this would also be a useful technique there.

APPENDIX - Estimating Variability

The variability of dioxin/furan blood lipid congener concentrations in the New Zealand was estimated based upon results from the 1996/1997 MfE organochlorine blood serum sampling programme. Due to the relatively small volumes of blood collected from participants, compared to volumes needed for testing, blood samples were pooled into larger sample units. Each sample was pooled in one of 80 strata used to categorise the sample population. Each stratum was defined with respect to gender, ethnicity, age, and locality. Individuals who were likely to have been occupationally exposed to organochlorines were excluded from the blood pooling. Each individual contributed an equal volume to the total pool blood serum volume.

A minimum pooled serum volume of 25ml was required for testing which required the contribution of 5ml from at least five individuals. In 20 of the 80 strata there were insufficient numbers to meet this criterion and no testing was conducted for these strata. However, in 16 strata there were sufficient numbers for two or three separate blood serum pools each of 25 individuals. A total of 80 blood serum pools were sent for testing. The number of individuals included in each blood serum pool varied from 5 to 47 individuals. A total of 1,834 samples (1,034 females and 800 males) of the total 2,497 eligible samples were included in pooled samples.

From the results of these pooled samples estimates of average dioxin concentrations present in the New Zealand population's blood lipid levels and the variability of dioxin concentration (i.e. standard deviation) have been derived. Estimates for the New Zealand population have been calculated for each of the five age and two gender grouping (i.e. a total ten population groupings). In the calculation of averages and standard deviations, results from the pooled blood samples have been weighted with respect to the number of participants included in each pooled sample. The calculation procedures is described below

Calculation of mean population congener concentrations

Weighted mean averages have been calculated using the following formula adapted from Bland & Kerry (1998):

$$x = (\sum n_i * c_i) / \sum n_i$$

Where:
x = weighted mean concentration of the pooled blood sample
ni = number of participant included in blood pool 'i'
ci = blood lipid congener concentration (ng/kg) in blood pool 'i'

Calculation of weight standard deviation

In estimating the standard deviation of the population based upon the congener concentrations of pooled samples, first the weighted standard deviation of the pooled sample concentration was calculated. This used the procedure described by Bland & Kerry (1998):

Initially the weighted sum of squares was calculated:

$$SS = (\sum n_i * c_i^2) / (\sum n_i / N)$$

Where:
SS = weighted sum of squares
ni = number of participant included in blood pool 'i'
ci = blood lipid congener concentration (ng/kg) in blood pool 'i'
N = the number of pooled samples

The variance is calculated by calculating the weight sum of squares about the mean and dividing this by the degrees of freedom (N-1).

$$Var = (SS - x^2*N) / (N-1)$$

The weighted standard deviation (s_X) of the pooled blood serum concentrations is the square root of the variance

$$s_X = Var^{0.5}$$

Consequently the standard error of the mean concentration can be estimated in the usual manner.

$$se(x) = s_X / N^{0.5}$$

There are two possible sources of variation in the collected blood serum dioxin concentration: the variation between-subjects or the "true" variation; and the variation within the subject, the measurement error. If it is assumed that the variation between subjects is much greater than the variation within subject then the standard error calculated using the weighted pool congener concentration would be approximately same as if blood serum congener concentrations were measured for each individual person included and the pooled results used to estimated the standard error (Bland, 2001).

Therefore, by knowing the standard error of the mean of the pooled samples it is possible to work back and estimated the standard deviation of the population based upon the total number of individuals included in each of the pooled blood samples.

$$s_{Total} = se(x) * N_{Total}^{0.5}$$

Where:
s_{Total} = estimated standard deviation of the population
se(x) = standard error of the weighted pooled blood sample concentrations number of
N_{Total} = total number of individual included in the pooled samples (i.e. $\sum n_i$)

It should be noted that this is only an estimate of the population standard deviation that is intended to provide an indication of expected degree of variability that be observed in population.

Bland JM, Kerry SM. 1998. Statistical Note: Weighted comparison of means. *British Medical Journal*, 1998;316:129 (10 January).

Bland JM. 2001. How does pooling blood samples affect standard deviation? www.sghms.ac.uk/depts/phs/staff/jmb/poolsamp.