Appendix K

1.1 STATISTICAL ASSESSMENT

The predicted serum levels using the McLachlan-based multi-pathway model have been analysed together with the data from the MfE serum survey to examine which age and gender groups are most likely to show a statistically significant increase in 2,3,7,8-TCDD concentrations in serum lipid. This analysis has focused on calculating the 95% confidence interval for the difference between the mean of the Paritutu group under consideration and the mean results for the MfE survey for the same group. If the lower bound of this 95% confidence interval exceeds zero, the mean concentration for the Paritutu group exceeds the mean concentration for the corresponding MfE group, at the 95% confidence level. That is, an "excess" level of 2,3,7,8-TCDD is indicated.

For this assessment, the top 10 predicted serum concentrations were selected for each age/gender group and the 95% confidence interval was calculated for the top 4, top 5 etc up to the top 10 concentrations. These calculations were set up so that a factor could be applied to the predicted serum concentrations, increasing or decreasing all of these from the McLachlan based predictions. This factor was adjusted to give the smallest percentage of the McLachlan concentrations consistent with the lower 95% confidence interval exceeding 0 for at least some of the groups of top concentrations.

Similar calculations were done for most of the age and gender groups, but omitting the highest of the McLachlan predictions. This was done because, for most of the groups, the single highest result was substantially larger than the remainder, probably because different exposure pathways are significant for these candidates, and can therefore reasonably be considered to be part of a different statistical population.

The table also shows the predicted 'ranking' of last candidate to be included in the analysis group. Different ranking scales were used for males and females.

Table 1 shows a summary of this analysis.

Age range (in 1997)	Gender	Highest single result	% of McLachlan for lower 95% CI of difference of means>0	Minimum No. of candidates required in group	M/F Ranking of Last Candidate
64+	Male	included	None	-	-
64+	Male	excluded	38%	4	13
64+	Female	included	110%	10	16
64+	Female	excluded	28%	4	7
50-64	Male	included	23%	4	8
50-64	Male	excluded	Not assessed		-
50-64	Female	included	35%	9	29
50-64	Female	excluded	24%	4	18
35-49	Male	included	80%	9	40
35-49	Male	excluded	33%	8	37
35-49	Female	included	32%	5	25
35-49	Female	excluded	16%	4	25

If the variability in the McLachlan-based predictions is a reasonable indication of the variability of the samples from the candidates, the smallest percentages and minimum number of candidates required in the group indicates the groups for which significant differences from the MfE survey means are likely to be found. On this basis, males in the 50-64 age group are those most likely to show statistically significant "excess" 2,3,7,8-TCDD. Women in the 64+ age group are about as likely as the male 50-64 age group to show a statistically significant "excess", particularly if the single very high top result is omitted.

It is proposed that the best strategy would be to select the top 10 females in the 64+ age group and the top 10 males in the 50-64 age group. Because of public interest, it would probably also be necessary to include the top male in the 64+ age group, because the three predicted concentration is so much higher than for other candidates.

This would then leave some samples out of a 25 first cut available for quality control, and perhaps some other selected individuals.

We must be cautious about placing too much weight on the variability indicated by the multi-pathway modelling, combined with the toxicokinetic model. The input parameters for the multi-pathway modelling (particularly the extent to which each exposure pathway applies) are at best approximate and the actual variability might be considerably greater than estimated here. However, the variability seems not unreasonable, since it is at a similar level on a percentage basis to that estimated for the MfE serum survey. This does appear to be the best approach to selecting first cut candidates.

2. MORE DETAILED OUT PUT FROM THE STATISTICAL ANALYSIS

Male	MfE group	65+						Difference in Mean			
		Adjustment factor	**1.0**				95% CI of mean			+/- 95% CI	
Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	min value	Diff in Means	SE of Diff	min	max
1057	1	1	134	134.4				131.4	0.1		
1360	2	4	29	81.7	74.4	52.6		78.7	52.6		
1154	3	7	20	61.1	63.6	36.7		58.1	36.7		
1550	4	11	16	49.7	56.7	28.4	-40.5	46.7	28.4	-44	137
1136	5	13	13	42.4	51.8	23.2	-21.9	39.4	23.2	-25	104
1455	6	19	12	37.3	48.0	19.6	-13.1	34.3	19.6	-16	85
1709	7	21	11	33.5	44.9	17.0	-8.1	30.5	17.0	-11	72
1151	8	25	8	30.3	42.6	15.0	-5.3	27.3	15.0	-8	63
1474	9	28	8	27.8	40.5	13.5	-3.3	24.8	13.5	-6	56
1705	10	29	7	25.8	38.7	12.2	-1.9	22.8	12.2	-5	50

	Excluding first value as an outlier							Difference in Mean			
		Adjustment factor	**0.38**				95% CI of mean	Diff in Means	SE of Diff	+/- 95% CI	
Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	min value			min	max
1360	1	4	29	11.1				8.0	0.1		
1154	2	7	20	9.3	2.5	1.8		6.3	1.8		
1550	3	11	16	8.2	2.6	1.5		5.1	1.5		
1136	4	13	13	7.4	2.7	1.3	3.1	4.3	1.3	0.1	8.6
1455	5	19	12	6.8	2.7	1.2	3.5	3.8	1.2	0.5	7.1
1709	6	21	11	6.3	2.6	1.1	3.6	3.3	1.1	0.5	6.1
1151	7	25	8	5.9	2.7	1.0	3.4	2.9	1.0	0.3	5.4
1474	8	28	8	5.5	2.7	1.0	3.2	2.5	1.0	0.2	4.8
1705	9	29	7	5.2	2.7	0.9	3.2	2.2	0.9	0.1	4.3
0	10	29	0	5.2	2.7	0.8	3.3	2.2	0.9	0.3	4.1

Male	MfE group	50-64						Difference in Mean			
		Adjustment factor	**0.23**				95% CI of mean			+/- 95% CI	
Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	min value	Diff in Means	SE of Diff	min	max
1567	1	3	28	6.4				3.9	0.1		
1314	2	5	20	5.4	1.3	0.9		2.9	1.0		
1046	3	6	19	5.1	1.1	0.7		2.5	0.7		
1106	4	8	14	4.6	1.3	0.6	2.6	2.1	0.7	0.0	4.2
1147	5	9	14	4.3	1.3	0.6	2.7	1.8	0.6	0.2	3.4
1047	6	10	16	4.2	1.2	0.5	3.0	1.7	0.5	0.5	3.0
1030	7	12	13	4.1	1.2	0.4	3.0	1.5	0.5	0.4	2.6
1261	8	14	13	3.9	1.2	0.4	3.0	1.4	0.4	0.4	2.4
1265	9	16	10	3.8	1.2	0.4	2.8	1.2	0.4	0.3	2.2
1368	10	18	10	3.6	1.2	0.4	2.7	1.1	0.4	0.2	2.0

Male **MfE group** **35-49** **Difference in Mean**

Adjustment factor 0.80

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	+/- 95% CI min	max
1058	1	2	41	32.8				31.1	0.1		
1687	2	15	11	20.7	17.1	12.1		18.9	12.1		
1447	3	17	10	16.4	14.2	8.2		14.7	8.2		
1674	4	22	9	14.1	12.5	6.2	-5.8	12.3	6.2	-7.5	32.2
1386	5	30	6	12.3	11.6	5.2	-2.1	10.5	5.2	-3.8	24.9
1672	6	31	6	11.0	10.8	4.4	-0.3	9.3	4.4	-2.0	20.6
1596	7	32	6	10.1	10.1	3.8	0.7	8.4	3.8	-1.0	17.7
1466	8	34	5	9.4	9.6	3.4	1.4	7.6	3.4	-0.4	15.7
1526	9	37	5	8.8	9.1	3.0	1.8	7.1	3.0	0.03	14.1
1294	10	40	4	8.3	8.8	2.8	2.0	6.5	2.8	0.3	12.8

Excluding first value as an outlier **Difference in Mean**

Adjustment factor 0.33

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	+/- 95% CI min	max
1687	1	15	11	3.5				1.8	0.1		
1447	2	17	10	3.4	0.2	0.1		1.6	0.2		
1674	3	22	9	3.2	0.3	0.2		1.5	0.2		
1386	4	30	6	2.9	0.6	0.3	1.9	1.2	0.3	0.1	2.3
1672	5	31	6	2.8	0.7	0.3	1.9	1.0	0.3	0.1	1.9
1596	6	32	6	2.6	0.7	0.3	1.9	0.8	0.3	0.0	1.6
1466	7	34	5	2.5	0.7	0.3	1.8	0.7	0.3	0.0	1.4
1526	8	37	5	2.4	0.7	0.3	1.8	0.6	0.3	0.0	1.3
1294	9	40	4	2.3	0.7	0.2	1.7	0.5	0.3	-0.1	1.2
1135	10	47	4	2.2	0.8	0.2	1.7	0.4	0.3	-0.2	1.0

Female   **MfE group**   **65+**

Difference in Mean

Adjustment factor   **1.10**

+/- 95% CI

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	min	max
1056	1	1	250	250				244.4	0.4		
1155	2	3	66	174	144	102		167.9	102		
1137	3	5	39	130	126	73		124.4	73		
1593	4	6	38	108	112	56	-70.7	102.2	56	-76.6	281
1614	5	7	36	94	102	46	-32.4	88.4	46	-38.3	215
1448	6	9	28	84	95	39	-15.8	77.9	39	-21.7	177
1513	7	10	27	76	89	34	-6.3	70.1	34	-12.2	152
1172	8	11	25	70	84	30	-0.3	64.1	30	-6.2	134
1574	9	12	25	65	80	27	3.8	59.3	27	-2.2	121
1385	10	16	22	61	77	24	6.5	55.3	24	0.5	110

Excluding first value as an outlier

Difference in Mean

Adjustment factor   **0.28**

+/- 95% CI

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	min	max
1155	1	3	66	18.4				12.5	0.4		
1137	2	5	39	14.7	5.3	3.7		8.8	3.7		
1593	3	6	38	13.3	4.4	2.5		7.4	2.6		
1614	4	7	36	12.5	4.0	2.0	6.2	6.6	2.0	0.1	13
1448	5	9	28	11.6	4.0	1.8	6.6	5.6	1.8	0.6	11
1513	6	10	27	10.9	3.9	1.6	6.8	5.0	1.7	0.7	9
1172	7	11	25	10.4	3.9	1.5	6.8	4.4	1.5	0.7	8
1574	8	12	25	9.9	3.8	1.3	6.8	4.0	1.4	0.7	7
1385	9	16	22	9.5	3.8	1.3	6.6	3.6	1.3	0.6	7
1491	10	23	17	9.0	3.9	1.2	6.3	3.1	1.3	0.2	6

Female	MfE group	50-64						**Difference in Mean**			
Adjustment factor		**0.35**					**95% CI of mean min value**			**+/- 95% CI**	
Candidate	**No in Sample**	**Rank**	**TCDD**	**mean**	**stdev**	**SE**		**Diff in Means**	**SE of Diff**	**min**	**max**
1627	1	2	90.4	31.6				28.1	0.4		
1031	2	8	31.4	21.3	14.6	10.3		17.8	10.3		
1145	3	13	23.3	16.9	12.8	7.4		13.4	7.4		
1358	4	15	22.3	14.6	11.4	5.7	-3.5	11.1	5.7	-7.1	29.3
1702	5	18	21.3	13.2	10.4	4.6	0.3	9.6	4.7	-3.3	22.6
1114	6	20	20.4	12.2	9.6	3.9	2.1	8.6	3.9	-1.5	18.8
1048	7	22	18.4	11.4	9.0	3.4	3.0	7.8	3.4	-0.6	16.2
1440	8	24	16.6	10.7	8.6	3.0	3.5	7.1	3.1	-0.1	14.4
1008	9	29	15.1	10.1	8.2	2.7	3.7	6.5	2.8	0.1	12.9
1134	10	36	13.1	9.5	8.0	2.5	3.8	6.0	2.5	0.2	11.7

	Excluding first value as an outlier							**Difference in Mean**			
Adjustment factor		**0.24**					**95% CI of mean min value**	**Diff in Means**	**SE of Diff**	**+/- 95% CI**	
Candidate	**No in Sample**	**Rank**	**TCDD**	**mean**	**stdev**	**SE**				**min**	**max**
1031	1	8	31.4	7.5				4.0	0.4		
1145	2	13	23.3	6.6	1.4	1.0		3.0	1.0		
1358	3	15	22.3	6.2	1.2	0.7		2.6	0.8		
1702	4	18	21.3	5.9	1.1	0.6	4.1	2.3	0.7	0.2	4.5
1114	5	20	20.4	5.7	1.1	0.5	4.4	2.1	0.6	0.5	3.8
1048	6	22	18.4	5.5	1.1	0.4	4.3	1.9	0.6	0.5	3.4
1440	7	24	16.6	5.3	1.1	0.4	4.2	1.7	0.6	0.3	3.1
1008	8	29	15.1	5.1	1.2	0.4	4.1	1.5	0.6	0.2	2.8
1134	9	36	13.1	4.9	1.3	0.4	3.9	1.3	0.6	0.0	2.6
0	10	36	0.0	4.9	1.3	0.4	3.9	1.3	0.5	0.1	2.5

Female **MfE group 3** **35-49**

Difference in Mean

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	+/- 95% CI min	max
	Adjustment factor		0.32								
1059	1	4	54.0	17.3				15.1	0.1		
1729	2	14	23.2	12.3	7.0	4.9		10.2	4.9		
1591	3	17	21.8	10.5	5.8	3.4		8.4	3.4		
1319	4	19	20.6	9.6	5.2	2.6	1.4	7.4	2.6	-0.8	15.6
1402	5	25	16.3	8.7	4.9	2.2	2.6	6.5	2.2	0.5	12.6
1039	6	30	15.0	8.0	4.6	1.9	3.2	5.9	1.9	1.0	10.8
1069	7	33	13.7	7.5	4.4	1.7	3.4	5.4	1.7	1.3	9.5
1728	8	35	13.6	7.1	4.3	1.5	3.5	5.0	1.5	1.4	8.6
1331	9	37	13.0	6.8	4.1	1.4	3.6	4.7	1.4	1.5	7.8
0	10	37	0.0	6.8	4.1	1.3	3.8	4.7	1.3	1.7	7.6

Excluding first value as an outlier

Difference in Mean

Candidate	No in Sample	Rank	TCDD	mean	stdev	SE	95% CI of mean min value	Diff in Means	SE of Diff	+/- 95% CI min	max
	Adjustment factor		0.16								
1729	1	14	23.2	3.7				1.6	0.1		
1591	2	17	21.8	3.6	0.2	0.1		1.5	0.2		
1319	3	19	20.6	3.5	0.2	0.1		1.4	0.2		
1402	4	25	16.3	3.3	0.5	0.2	2.5	1.1	0.3	0.3	2.0
1039	5	30	15.0	3.1	0.6	0.3	2.4	1.0	0.3	0.2	1.7
1069	6	33	13.7	2.9	0.6	0.3	2.3	0.8	0.3	0.1	1.5
1728	7	35	13.6	2.8	0.6	0.2	2.2	0.7	0.3	0.0	1.4
1331	8	37	13.0	2.7	0.7	0.2	2.2	0.6	0.3	0.0	1.2
0	9	37	0.0	2.7	0.7	0.2	2.2	0.6	0.2	0.0	1.2
0	10	37	0.0	2.7	0.7	0.2	2.3	0.6	0.2	0.1	1.1