

TCDD exposures in Paritutu, New Zealand

A review of the commentary by J. Leonard (Gerry Rea Associates) on the 2005 Institute of Environmental Sciences and Research (ESR) report to NZ Ministry of Health entitled A study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) Exposures in Paritutu, New Zealand.

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Brief

To provide statistical comment on the review conducted by J. Leonard (Accountant) of the ESR report 'A study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) Exposures in Paritutu, New Zealand (2005). My comments are restricted to J. Leonard's review and do not represent a full appraisal of the ESR report. I have had access to all relevant appendices associated with the 2005 report, including appendix O which tables the anonymised raw TCDD data. I have restricted my focus to the 2005 ESR report, having noted that although some of J. Leonard's comments relate to the 2004 report these minor issues have largely been addressed in the 2005 report and the later report containing data collected in late 2004, appears to largely supersede the earlier report.

Leonard commentary

The body of the commentary by J. Leonard is structured in a semi-legal manner largely meaning that each sentence becomes a bullet point and single comments are often spread through several bullet points. The executive summary however, includes 8 largely independent comments, each of which is broadly based on a collection of numbered bullet points contained within the body of the text. It appears therefore, that executive summary point 2.1 relates to section 7, 2.2 to section 8 etc, this structure however, for some reason does not apply to executive summary points 2.7 and 2.8. The numbering within section 12 is also confusing with each point appearing to constitute an independent section. In light of this I have chosen to comment specifically on the key points as

outlined in the executive summary, paying heed to the specific points within the body of the text which appear to relate to these key points.

Overview

The 2005 ESR report summarises work undertaken between October 2001 and January 2005, to investigate 'non-occupational exposure to dioxins among residents of Paritutu'. The authors have sensibly chosen to address this issue by targeting for assessment only those individuals *likely* to have been most exposed to non-occupational sources of Dioxin. The logic here, and one often used in such circumstances is that if these individuals do not have elevated levels then one can reasonably conclude that non-occupational exposure in this locality is not an issue. The drawbacks however, with such designs is that the actual extent of elevated dioxin levels in the whole community is not directly quantified and that the selection of 'high-risk' individuals is based on estimates of exposure not actual exposures. These critical points I believe have not been grasped in the Leonard review and the report must be considered within this contextual framework. Additionally, quantifying retrospective exposures and retrospective toxin levels and thereby establishing a cause-effect association for a putative toxin source poses numerous challenges for epidemiologists. Specific to the Dioxin problem are the air-dispersion modeling, the spatial modeling of soil levels, the multi-pathway modeling of exposure from multiple sources, and the toxicokinetic model. Much of the report (and appendices) deals with these models and results pertinent to these standard epidemiological challenges. These undertakings and results however, are largely ignored in the Leonard review which focuses on only a small part of the study.

A further important point to consider when appraising epidemiological studies is the role of confounding within the putative cause-effect association. Within the Paritutu scenario, the role of age, years of exposure and timing of exposure are very likely to confound. Older people are more likely to have been exposed for longer and are more likely to have been exposed within the earlier period of the plant. Extricating the independent effects of these 3 factors is not straight-forward and does require significant sample sizes chosen

appropriately. This study does not attempt to unravel this problem and could not have done.

Comments

The Leonard review outlines 8 points in the executive summary. Three of these I consider important and contentious, the remaining five are minor and are covered in less detail below.

1. (Ref 2.1) ‘The sample sizes are very small considering the variability of the samples and considering the conclusions the study is endeavoring to reach.’ The sample size (n=52) is small. However, the primary purpose of the sampling was to establish if there were elevated levels due to non-occupational exposure. For this purpose the sample size is small –but adequate. Leonard’s review does not dispute the point that measured levels among the 52 individuals are elevated, most probably as a consequence of non-occupational exposure. However, as soon as this sample is broken into age, gender, or exposure-history sub-groups to explore specific associations then the small sample size becomes very evident and confidence intervals are wide as stated. I believe that the conclusions drawn in the report in relation to the effects within specific sub-groups are sufficiently cautious and I’m sure the authors would agree that these effects require confirmation with larger sample sizes. I note Leonard’s incorrect assertion that accuracy is related to sample size, -precision relates to sample size.

2. (Ref 2.2) ‘There has been a mixing of data between two sets of data that should not have occurred that is misleading and may have lead to incorrect conclusions.’ This represents a very provocative and unsubstantiated claim. Presumably this is in reference to the combining of data from Parts I and II (sampled on different dates) of the serum sampling. These data had to and should have been combined. Leonard states ‘The date on which the data is collected is irrelevant’. Collectively the data can then address issues of age, gender, exposures years and exposure within particular periods. Individually, the two parts could not address these questions. It is possible that the objection arises from the inclusion of 4 participants in Part II summaries when they were selected under the criteria

for Part I. The authors clearly indicate that the summaries relate to Parts I and II and DO NOT make claims on timing of exposure based purely on Tables 2 & 3 (which summarise the levels from the two Parts). Note that the only difference in the criteria for selection between the two parts was the timing of residence, Part II to only include those exposed after 1973. The arithmetic manipulations (8.5-8.11) undertaken perhaps to create 'exposure period' tables are irrelevant for two reasons. Firstly, no claims are made in relation to the extent of the elevation in levels from tables 2 and 3 and secondly we do not know what age-gender sub-groups the remaining two participants (2 of the 4) belong to.

3. (Ref 2.3) 'The data on which the conclusions have been reached in the study in relation to exposure occurring in the two different phases of the plant operation (Pre 1974 and Post 1974) are not evidenced in the reports.' The 2005 report makes no such claims and reports that the comparison of 2.6pg/g vs 1.5pg/g (pre-1974 vs post-1974) for those with < 15 years residence is not statistically significant. Why it is suggested (9.3) that the four Pre-1974 individuals (from Part II) might be erroneously categorised into the Post-1974 group is not clear. Equally, why the combining of the two data sets (9.9) should make conclusions on pre-1974 exposure impossible is also not clear.

Point by point review of Items 2.4 -2.8 (Executive summary).

2.4. Presumably a valid correction in the later report.

2.5. I presume this is relating to the relative contributions of exposed, non-exposed fruit and vegetables, poultry, eggs and kaimoana. I don't see any inconsistency between the two statements 11.7 and 11.8. both statements do not state that there is no link, (as Leonard indicates the data was insufficient to make this claim) but both correctly report that no association was found.

2.6 This comment appears to derive from the confusion over the terms 'duration of residence' and 'years of exposure'. This appears to be clarified in the 2005 report where Figure 4 (based appropriately on all 52 subjects) shows levels by 'years of exposure'. The

comparison of the two exposure groups (prior to 1974 and post 1974) among those exposed for less than 15 years, adds correctly to 37 subjects who are again sensibly derived from both the Part I and Part II samples -without deduction

2.7. It is unclear why these calculations have been undertaken and what point is being made. It appears that Leonard is not aware that half-life curves with identical half-lives maintain proportionality. So that the 7.4* and 4.3* figures are directly calculable from tables 4 and 5 (2004 figures) without the curves he has drawn. The equation (22.4) is in error.

2.8 A fair point. A biostatistician/epidemiologist could have usefully added to the report, however, none of the key findings would change.

Summary

I can find nothing within the commentary by Leonard that invalidates claims made from the 2005 ESR report. While I do not have access to Leonard's Curriculum Vitae, it is very clear from his commentary that he lacks the appropriate expertise and experience to make a sensible, and reasonable appraisal of scientific research of this type. I am dismayed therefore, that this commentary has caused so much furore, when in the first instance the ESR 2005 report was appropriately and sensibly peer- reviewed by Independent, National and International experts who have a familiarity with epidemiological study design, analysis and interpretation. Major limitations within this important study would certainly have been identified by these reviewers.

C Frampton (12/11/2006)