APPENDIX H

PEER REVIEW COMMENTS, HEALTH CANADA COMMENTS AND CANTOX ENVIRONMENTAL RESPONSE TO COMMENTS

Peer Review of Task 3A-1: Toxicological Risk Assessment Pertaining to Potential Occupational and Related Exposures Associated with Herbicide Spraying Operations at CFB Gagetown – Tier 1 – 1966-67 U.S. Trials – Manufacturing Impurities (Contaminants)

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Introduction:

This review was conducted in accordance with the Terms of Reference for the Peer Review of The Toxicological Risk Assessment Pertaining to Potential Occupational and Related Exposures Associated with Herbicide Spraying Operations at Canadian Forces Base (CFB) Gagetown from 1952 to Present: Task 3A.1, Tier 1, a document prepared by Health Canada describing the peer review process for risk assessment reports addressing human exposures and potential health hazards associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin and hexachlorobenzene, two manufacturing impurities present in herbicides sprayed at CFB Gagetown for three days in June 1966 and four days in June 1967.

Overall Comments:

The report appears to summarize a well-researched and scientifically defensible assessment of potential health risks. Cantox has demonstrated a high degree of creativity and knowledge in their application of the various scientific tools available for the estimation of risks from the contaminants of concern. Notwithstanding the above, several issues should be resolved prior to giving full endorsement of the methods, results, and conclusions.

Assessment:

Our overall opinion is that the report is acceptable with major revision (as outlined).

Major Issues:

1) **Exposure Estimates**

Issue:
From our perspective, there does not appear to be enough information provided to arrive at the same exposure estimates that are reported in Tables 5-12 to 5-17. We have tried to verify the estimated exposures in "ng/kg bw" and have not been able to arrive at the same values. More specifically, when we completed the exposure calculations using the supplied information, we arrived at different exposure estimates for the following receptors:

- Mixer/Loader Accident 1966 Scenario: Using the Cantox data and equations to the fullest extent possible, our estimate for *high end* exposure to PCDD is 7,300 ng/kg/day (for 3 days) versus 5,100 ng/kg (presumably for each of 3 days but this is not specified) estimated by Cantox. For HCB, our estimate for *central* exposure is 5,600 ng/kg/day (for 3 days) versus 394 ng/kg (presumably for each of 3 days) estimated by Cantox. The Appendix provides the assumptions that were used in our worked example calculations.

- Mixer/Loader Routine 1967 Scenario: Using the Cantox data and equations to the fullest extent possible, our estimate for *high-end* exposure to PCDD is 0.042 ng/kg for each day versus 0.77 ng/kg (presumably for each day) estimated by Cantox. The Appendix provides the assumptions that were used in our worked example calculations.

- Field Scout 1967 Scenario: Using the Cantox data and equations to the fullest extent possible, our estimate for *high-end* exposure to PCDD is 2 ng/kg/event versus 0.030 ng/kg/event estimated by Cantox. The Appendix provides the assumptions that were used in our worked example calculations.

It is stressed that it is possible that we have erred in our review but these and all other calculations in the report should be resolved prior to finalization of the report. In making these calculations, we found ourselves having to guess at certain assumptions or parameter values and it is possible that further clarification by Cantox would provide the reasons why we could not reproduced their exposure estimates. Of fundamental importance to the entire assessment, we did not have access to the PHED database and so were unable to check the PHED Unit Exposure Values summarized in Tables 5-6, 5-7 and 5-8. We suggest that Cantox show by example how they arrived at the some of the values in these critical tables.

Recommendation:
It is recommended that:

- Cantox review all of their calculations to ensure that no errors were made;
- Cantox should provide worked examples of their calculations (perhaps in an Appendix) showing the detail of their calculations, assumptions, and parameter values, for each of the receptors; and
- Cantox should ensure that all parameter values used in the formulae are provided in a separate table so that, together with the worked examples, any reader can reproduce their results.
- Illustrate by example the determination of some of the PHED Unit Exposure Values summarized in Tables 5-6, 5-7 and 5-8.

2) Background Exposure Estimates

Issue:
An article by Lorber (2002) has suggested that average background dioxin-TEQ serum lipid concentrations in the US were between 50 ppt and 80 ppt during the 1970's whereas Cantox has used a value of 21.8 ppt. It is unclear if the Lorber paper is more accurate than the Cantox estimate and/or perhaps included other considerations. Nevertheless, if the Lorber value was used in the assessment, it is possible that appreciably different results would have been found (e.g., values in Table 7-1 would need to be revisited).

Recommendation:
It is recommended that Cantox review the Lorber (2002) paper and any other data that may relevant to serum lipid concentrations around the time of the exposure events. If revised background exposure estimates are recommended, the interpretation of the risk assessment may need to be revisited.

3) Inclusion of Dioxin-Like PCBs in Background Exposure Estimates

Issue:
Somewhat related to the above, it is possible that dioxin-like PCBs may have contributed to the typical background exposures that receptors may have been receiving at the time of the spraying events. In some cases, dioxin-like PCB exposures may contribute appreciably and, thus, should possibly be considered or discussed in the Cantox report.

Recommendation:
It is recommended that Cantox review and comment on whether inclusion of dioxin-like PCB data may have altered their results and conclusions.

4) Risk Calculations

Issue:
If exposure estimates are found to require recalculation, then the Cantox risk estimates provided in Tables 7-2 to 7-24 and Figures 7-1 to 7-5 may need to be revisited. Currently, the risk estimates are reproducible only if the exposure estimates presented in earlier tables are accurate.

Recommendation:
Based on the outcome of the re-evaluation of exposure estimates, it is recommended that Cantox re-evaluate the risk calculations.

5) Discussion

Issue:
Stakeholders, health officials, and policy makers will want to know how these risks compare with those experienced by individuals in other cohorts, such as victims of the Seveso accident, industrial workers who made herbicides, agricultural workers who sprayed herbicides, or U.S. Air Force veterans of Operation Ranch Hand, the unit responsible for spraying Agent Orange and other herbicides in Vietnam.

Recommendation:
Expand Chapter 9 to put the risk estimates into perspective by comparing some of the CFB Gagetown risks with those that may have been experienced by individuals in other cohorts. Strengthen the discussion by mentioning that the high Mixer/Loader exposure estimates (some exceed baseline by 80 times) are consistent with your simulation (summarized in Appendix D) and with exposure estimates in Ranch Hand ground crew. The Ranch Hand ground crew loaded spray tanks in aircraft with Agent Orange and other herbicides and so functioned in some ways like your Mixer/loader receptors [Michalek JE, Wolfe WH, Miner JC, Papa TM and Pirkle JL. Indices of TCDD exposure and TCDD body burden in veterans of Operation Ranch Hand. *Journal of Exposure Analysis and Environmental Epidemiology* 1995;5(2):209-223].

6) Executive Summary

Issue:
Many readers will immediately look for the bottom line (on page ix) and will seek confirmation that the overall interpretations in the Executive Summary are consistent with material presented later. As currently written, the executive summary on page ix is not written with as much conviction as the bulleted items on pages 92 and 93.

Recommendation:
Replace the current six bulleted items on page ix of the Executive Summary with the eight bulleted items from pages 92 and 93.

Point-by-Point Review:

Report Title: It may be unavoidable but the report title is long and complex. If possible, a more concise title may be useful.

ES-2.0, Page ii, item 4: Replace "include" with "included".

Figure ES-1, Page iii and Figure 2-1, page 3: Black and white copes of the report do not show areas in "blue" and "green". It should be ensured that a color copy of this figure is provided in the version of the report that is circulated to stakeholders.

ES-4.0, Page v, item 1, first sentence: Replace "individuals are responsible" with "individuals were responsible".

ES-4.0, Page v, item 1, third sentence: Replace "may come" with "may have come".

ES-4.0, Page v, item 2, first sentence: Replace "individuals are responsible" with "individuals were responsible".

ES-4.0, Page v, item 2, third sentence: Replace "may be exposed" with "may have been exposed".

ES-4.0, Page v, item 3, first sentence: Replace "individuals are responsible" with "individuals were responsible".

ES-4.0, Page v, item 3, second sentence: Replace "may come" with "may have come".

ES-4.0, Page v, item 4, first sentence: Replace "may spend" with "may have spent".

ES-4.0, Page v, item 4, second sentence: Replace "may come" with "may have come".

ES-4.0, Page v, item 4, third sentence: Replace "accidentally be sprayed" with "accidentally have been sprayed".

ES-4.0, Page v, item 5, first sentence: Replace "may live" with "may have lived" and "occasionally use" with "occasionally used".

ES-4.0, Page v: On this page and also elsewhere in the report the term "Mixer/Loader/Applicator" is used as if it was one receptor when in the risk calculations Cantox separately estimated risks for the "Mixer/Loader" and then the "Applicator". It is suggested that the term "Mixer/Loader/Applicator" not be used as a single group or if it is, exposure and risk calculations should be summed for all of these activities to more accurately reflect this group (also see Section 4.2, page 13).

ES-4.0, Page v: Off-site civilians should not be in a bulleted list is introduced as "the following groups of people were assessed" (since it is clear they were not assessed in

TIER 1). We suggest that you mention in a separate paragraph that this group will be addressed in the TIER 2 and 3 assessments.

ES-5.0, page vi: It would be helpful to summarize the exposure routes and scenarios that were evaluated. We suggest that you expand the paragraph to mention the dermal and inhalation routes in the routine and accidental exposure scenarios that you develop in Chapter 7.

ES-6.0, Page vii, paragraph beginning "Based on epidemiological evidence…", first sentence: Replace "link" with "association".

ES-6.0, Page vii, paragraph beginning "There is only limited evidence…" first sentence: Replace "link" with "association".

ES-6.0, Page vii, paragraph beginning "There is only limited evidence…" sixth item: Replace "mellitis" with "mellitus".

ES-6.0, Page viii, paragraph beginning "There is inadequate …": Replace "link" with "association".

ES-7.0, Page ix. Replace the six bulleted items in this section with the eight bulleted items on pages 92 and 93. Revise the paragraph beginning "The mixer/loader/applicator, …" to introduce the eight bulleted items from pages 92 and 93.

Section 2.0, Page 4: Demaree and Creager (1968) reference is cited as Demaree and Creager (1968a) in reference section.

Section 2.0, Page 5: Is any information available on weather conditions during the spraying event? We are not sure if this would affect any exposure estimate but it could be presented or at least mentioned.

Section 2.0, Pages 5 and 6: Number of gallons of active ingredient used per acre does not seem to be provided but would be useful in these locations.

Section 2.0, Page 6: Third line from top of page, "hcbcontaminant" should be "HCB contaminant".

Tables 2-1 and 2-2, Page 6: Do concentrations presented in "ppm" refer to mass:mass (i.e., mg/kg) or mass:volume (i.e., mg/L)? Have appropriate corrections for density been completed if the latter is the case (these would be important to subsequent exposure calculations)? For example, in the case of PCDD in 2,4,5-T, 45 mg/kg would correspond to 81 mg/L (if a density of 1.8 g/mL was assumed) while 45 mg/L would correspond to 25 mg/kg. These are important values used in the exposure equations and it should be verified whether "ppm" referred to "mg/kg" or "mg/L" and that they were used appropriately in the risk assessment. The resolution of "ppm" as mass:mass or

mass:volume should be clearly specified in the paragraph preceding Tables 2-1 and 2-2 because "ppm" appears throughout the report.

In these tables, it may also be useful to indicate whether or not the concentration value provided represents a mean or maximum value (since a combination of values are provided).

Finally, it may be important to specify if these concentrations are specific to the herbicide or the active ingredient in the herbicide. For example, does 45 ppm represent the concentration of TCDD in 2,4,5-T? Or does it represent the concentration in Agent Orange? Some of the information provided later in the report would suggest the former but this should be specified. Does this potentially affect exposure calculations for the Mixer/Loader spill scenario?

Section 3.3.1, Page 9, paragraph beginning "Where available …", last sentence, "RfC" is probably "Reference Concentration", please define parenthetically.

Section 3.4, Page 10: Perhaps present the equation for Exposure Ratio or Hazard Quotient as one or the other (but not both, since it could be a bit confusing for some). Also, in the example equation the units are provided as "μg/kg/day" while throughout the report exposure estimates are provided with units as "ng/kg", "ng/kg/day", "ng/kg/event", "pg/kg", "pg/kg/day" and "pg/kg/event". In order to avoid confusion, it is recommended that Cantox consider the following:

- use one of "μg", "ng" or "pg" and then primarily only that value;
- whenever a dose rate is provided, use terms where it is clear that rates are mass per kilogram body weight per day (e.g., 5,100 ng/kg bw/day) to avoid confusion with body concentrations that can be expressed as mass per kilogram (e.g., 5,100 ng/kg);
- adopt consistent terminology for "2,3,7,8-TCDD", "dioxin", "TCDD", "TEQ", "PCDD" and "dioxins" and then try to use just the one term if possible.

Section 3.4, Page 10: Here and elsewhere, it would be helpful if equations were numbered by chapter, using parallel notation with the figures, such as "equation 5-1".

Section 3.4.2, Page 12, paragraph beginning "The utility of the …", sentence beginning "ILCR estimates…" (near the bottom): Replace "provided by comparing the cancer slope factor" with "provided by multiplying the cancer slope factor".

Section 4.2, Page 13, paragraph beginning "The following…": Replace "might encounter" with "might have encountered".

Section 4.2, Page 13, paragraph beginning “The following…”, item 1, first and second sentences: Replace “are responsible” with “were responsible” and “It is anticipated” with “It is assumed”.

Section 4.2, Page 14, top of the page, item 2, second and third sentences: Replace “It was anticipated” with “It was assumed” and “It was assumed” with “It was also assumed”.

Section 4.2, Page 14, item 3, first and second sentences: Replace “individuals are responsible” with “individuals were responsible” and “It was anticipated” with “It was assumed”.

Section 4.2, Page 14, item 3 last sentence: Replace “impacted by the” with “contaminated by the”.

Section 4.2, Page 14, item 4, first and second sentences: Replace “personnel are those” with “personnel were those” and “may spend” with “may have spent” and “It was anticipated” with “It was assumed” and “would come into” with “would have come into”, and “which have been impacted” with “which have been contaminated”.

Section 4.2, Page 14, item 5, first and second sentences: Replace “individuals are those who may live near” with “individuals were those who may have lived near”, and “It was anticipated” with “It was assumed” and “which have been impacted” with “which have been contaminated”.

Figure 4-1, Page 15, right hand side: In the legend, Cantox should perhaps signify that “X” means no pathway while the checkmark notes an operable pathway. It is also unclear what the brackets around the checkmark signifies in the figure.

Figure 4-2, Page 16: Perhaps all receptors (not just mixer/loader) could be labeled.

Section 4.3.1.2, Page 19, paragraph beginning “Since the flagger… “, second sentence: Replace “This may occur” with “This may have occurred”.

Section 4.3.1.2, Page 19, paragraph beginning “Since the flagger…”, next-to-last sentence: Replace “accomplished Army” with “accomplished by Army”.

Section 4.3.1.2, Page 19, paragraph beginning “Additional potential exposure…”, last sentence: Replace “these exposure will be” with “these activities will be”.

Section 4.3.1.3, Page 20, paragraph beginning “Historical levels…”, sentence beginning “As a result of…”: Replace “food items may be” with “food items may have been”. Last sentence: Replace “Exposure to COCs also” with “Exposure to COCs may have also”.

Section 4.3.1.5, Page 20, paragraph beginning “Civilian receptors …”, second sentence: Replace “impacted” with “contaminated”.

Section 4.3.1.5, Page 20, paragraph beginning "Civilian receptors may also…", first and third sentences: Replace "may also be exposed" with "may also have been exposed" and "Impacted ground water" with "Contaminated ground water".

Section 5.1.1, Page 22: Unsure if these historical exposure estimates correspond with estimates provided by Lorber (2002). See our comment on Section 7.1, page 67.

Tables 5-1 and 5-2: There are two Table 5-1's (see pages 22 and 24) and two Table 5-2's (see pages 23 and 26).

Section 5.3.1.2, Page 25, top of the page, fourth line: Replace "According SERA" with "According to SERA".

Table 5-2, Page 26: All acronyms (e.g., "D", "T" and "a.i.") should be defined in the table so that the table is as stand alone as possible.

Tables 5-2 to 5-5, Pages 26 to 28: These tables present application rates in "g/m^2" whereas exposure calculations use units of "lbs/acre". Could these be harmonized in some manner? Or at least at a minimum, emphasize the conversion factor of "0.11 $g/lbs \times acres/m^2$" on page 26.

Section 5.4.1.1, Page 29, below Table 5-6, formulas for dermal routine exposure and inhalation from routine exposure: Please provide a literature references for this formulas. If Cantox derived them from first principles, please so state and give the rationale. Perhaps (as stated on page 23) these formulas and all other formulas used in this section (through page 39) are taken from reports by the PMRA, Health Canada, the US Bureau of Land Management, or the US Department of Agriculture. If so, then please ignore this comment. If not, please document or explain.

Section 5.4.1.1, Page 29: The equations presented on this page uses several parameters for which it is hard to determine which values were actually selected for use by Cantox. Specifically, the following parameters were not easily defined when we attempted to confirm Cantox's calculations:

> Application Rate (AR): Tables 5-2 to 5-5 provide the AR's but it is unclear which values were precisely used for the low, central and high exposure estimates.
>
> Area Treated (AT): It is unclear how many acres per day were assumed for the low, central and high exposure scenarios.
>
> Proportion of Dose Absorbed (P): Table 5-9 on page 34 apparently provides the values that were used but should likely be cited earlier (it is unclear to the reader that these values are available until 5 pages later in the report).

Body Weight (BW): Table 5-9 on page 34 apparently provides the value that was used but should likely be cited earlier (it is unclear to the reader that these values are available until 5 pages later in the report).

A summary table that provides the actual values selected for the low, central and high exposure scenarios would greatly clarify the risk assessment (and allow us to confirm the results of the risk assessment). (Note: This comment applies to all receptors not just Mixer/Loader.)

Section 5.4.1.2, Page 30, paragraph beginning "In addition to…", third sentence: Replace "concentrate" with "herbicide mixture".

Section 5.4.1.2, Page 30: The equations presented on this page uses several parameters for which it is hard to determine which values were actually selected for use by Cantox. In addition to the need to identify the previously mentioned parameters, the following parameters were not easily defined when we attempted to confirm Cantox's calculations:

Spill Amount (S): Unclear what the reference is for 0.5 L/day

Concentration of PCDD or HCB in Concentrate (AC): Unclear which values of these chemicals were used in units of "g/L"

A summary table that provides the actual values selected for the low, central and high exposure scenarios would greatly clarify the risk assessment (and would also allow us or any other reader to confirm the results of the risk assessment).

The reference for ENSR (2005) is not provided in the reference section.

Table 5-9, Page 34: The dermal absorption factors cited on this page should be discussed more fully. In particular, the proportion of absorbed dose cited by SERA (2001) could be discussed further since the reference for this value is not apparently available from a peer-reviewed journal. It is noted that alternate values for dermal absorption are available which include:

- Health Canada (2004) Preliminary Quantitative Risk Assessment cites a relative dermal absorption of 0.13 for hexachlorobenzene (no value provided for PCDD but many organic chemicals have values cited by Health Canada that are in the range of 0.1 to 0.2 and, thus, are greater than the values cited in Table 5-9); and

- ORNL (2006) cites a dermal absorption value of 0.03 for 2,3,7,8-TCDD and 0.01 for hexachlorobenzene.

It is important to note that we are not suggesting that the above listed values are more appropriate for use in the risk assessment. Instead, because it is a relatively sensitive parameter (i.e., dermal absorption is the major route of exposure for the Mixer/Loader which is the receptor driving the results of the assessment), we are suggesting that these

values and their derivation could be more precisely described and any uncertainties specified.

In the case of the values cited for PCDD, it should also be clarified that these are specific to 2,3,7,8-TCDD rather than representing a combined PCDD value.
The Cantox evaluation has been based on data that is specific to the general population (both sexes). If it is known that only men were using the area, it may be possible to revise the assessment based on male-specific data. Since Health Canada (2004) obtained much information from Richardson (1997) (which provides data for male, female and both sexes combined), it may be a relatively straightforward approach to base the risk assessment on male-specific endpoints. It should be stressed, however, that we have not been provided with any information that suggest only males were present.

Section 5.4.4, Page 36: The Application Rate in the Disolodgeable Residue calculation (note: misspelling of dislodgeable, an extra "o" is included) is in yet another different unit (i.e., $\mu g/m^2$) that is not provided in the tables. To avoid confusion, it is recommended that units be used that are similar to those previously provided (or a conversion factor provided).

Section 5.4.4, Page 36, formula for the transfer rate: The log is probably base 10. Please indicate the base of the logarithm.

Section 5.4.5, Page 38: Providing the results of the soil and berry concentration estimates would be interesting and make the risk assessment more clear.

Section 5.4.5, Page 38, third equation: The units do not balance, indicating the need for a conversion factor. Please check this equation.

It is also not immediately clear which soil half-life values were used in the risk assessment or what was the absorption factor for the chemicals via berry consumption (i.e., should not be as low as that from soil ingestion).

Perhaps the berry consumption rate could be provided as the number of servings per week.

Section 5.4.5, Page 39, first and second equations: The units do not balance, indicating the need for a conversion factor. Please check these equations.

Tables 5-12 through 5-17 Pages 41 to 44: As noted earlier, the exposure estimates provided in this table could not be reproduced with the information provided. It is highly recommended that these exposure estimates be validated by Cantox.

A separate issue is that the exposure estimates are provided as "ng/kg" or "ng/kg/event", and it is recommended that the precise units be provided. From the risk calculations, it appears that the units for all tables were "ng/kg bw/day" but it is not immediately obvious from the text. It is recommended that units be precisely provided in all cases.

A discussion on why exposure estimates vary amongst the various receptors between the various years would also be useful. Re-iterate that the reduced exposure in 1967 are due to Agent Purple not being used.

Section 6.1.2, Page 47, paragraph beginning "Wherever possible…": Insert a blank line to separate this paragraph from the preceding paragraph.

Section 6.2.4, Page 54-55: The chronic TDI for PCDD was chosen to be 2 pg/kg bw/day and is cited as Health Canada (2004; 2005). Although we cannot confirm it, we believe that the TDI provided in Health Canada (2004) was a slight error and that the intended value should have been 2.3 pg/kg bw/day (as opposed to 2.0 pg/kg bw/day) since it cites the JECFA assessment. Health Canada (2005) cited by Cantox actually provides a value of 2.3 pg/kg bw/day (not 2.0 pg/kg bw/day). Although it is likely only to have a minor effect, it is recommended that Cantox use a value of 2.3 pg/kg bw/day (as 2,3,7,8-TCDD TEQs) as the chronic TDI for PCDD.

With the above noted, the Body Burden$_{TRV}$ may change from 24.2 pg/g lipid to 27.7 pg/g lipid if the revised chronic TDI is used. However, since the TDI is expressed to 2 significant figures, this would likely be rounded to 28 pg/g lipid.

Tables 6-2 and 6-3, Page 55: As discussed earlier, it would be useful to provide dose rates in units that are similar to those used in earlier estimates.

In the case of body burden, the units should be more explicitly indicated (i.e., "kg body weight"? or "pg/g lipid" to be more consistent with the Body Burden$_{TRV}$).

The use of significant figures may be inappropriate in some of these tables (i.e., were some of the estimates in Table 6-3 really expressed to 5 significant figures?).

In Table 6-3, NR should be defined.

Section 6.3, Page 60, paragraph beginning "An analysis of the results…", sentence beginning "The only new study …": Please cite Akhtar F, Garabrant DH, Ketchum NS, and Michalek JE. Cancer in US Air Force veterans of the Vietnam War. *Journal of Occupational and Environmental Medicine* 2004;46(2):123-136.

Section 6.3, Page 60, paragraph beginning "Studies of Vietnam veterans…", sentence beginning "The Ranch Hand study …": Please cite a reference.

Section 6.3, Page 61, (first) paragraph beginning "Overall, the evidence of …", second sentence: Please cite Pavuk M, Michalek JE, and Schecter A. Prostate cancer in US Air Force veterans of the Vietnam War. J Expo Sci Environ Epidemiol. 2006 Mar;16(2):184-90. The relative risk was 2.27 for prostate cancer in the high dioxin category, hence the paragraph needs editing. Delete the first sentence of the paragraph and rewrite the second sentence as "The Ranch Hand studies showed an excess of prostate cancer in Ranch Hand veterans with elevated dioxin levels who served prior to 1969".

Section 6.3.2, Page 63, paragraph beginning "Evidence is suggestive …", sixth bullet: Replace "mellitis" with "mellitus".

Table 6-8, Page 66: Define GM.

Table 6-9, Page 66: As discussed earlier, the chronic TDI for PCDD should be revised. In addition, the more common term throughout the document has been TDI but in this table RfD is being used. It is recommended that the term TDI be used.

With respect to the term "Body Burden" it is recommended that the term "Body $Burden_{TRV}$" be used. In addition, the value provided in the table is 22.4 pg/g lipid whereas in prior text a value of 24.2 pg/g lipid was cited by Cantox. In any event, a revised value of 28 pg/g lipid would seem to be more appropriate if a chronic TDI of 2.3 pg/kg bw/day is adopted.

Section 7.1, Page 67, formula for D near the bottom of the page: The inversion of this formula appears to estimate the concentration of dioxin TEQ, not dioxin, in human tissue (pg TEQ/g) because the value estimated from it for the general population (at the top of page 68), 21.8 pg/g, is near the TEQ range previously cited on page 57, ie 22.8-32.7 ppt TEQ and because the ordinate of Figure 7-1 is cited as TEQ pg/kg/day. Please clarify the units for the concentration of dioxin. The half-life should be denoted as $t_{1/2}$ rather than $T_{1/2}$. As a check on your calculation of 21.8 pg/g, we used a simple one-compartment first order pharmacokinetic model and an EDI value of 1.8 pg TEQ/kg/day (rounded from your EDI of 1.76 pg TEQ/kg/day in Table 5-1) to arrive at an estimated steady state concentration of 20.7 pg/g lipid, relatively close to your value. Please comment in Section 5.1.1 on your EDI of 1.76 pg TEQ/kg/day, relative to the calculations summarized in Figure 6 of Lorber (2002).

Section 7.1, Page 68, paragraph beginning "Using a body burden …", please cite a reference for the half-life of 7.1 years. One such is Wolfe WH, Michalek JE, Miner JC, Patterson DG, Needham LL and Pirkle JL. Serum dioxin levels in Air Force Health Study participants preliminary report. *Morbidity Mortality Weekly Report* 1988;37:309-311. If this citation is correct, then the half-life estimate of 7.1 years was derived from repeatedly measured dioxin (pg/g lipid) in Vietnam veterans, whereas the application of it in the subsequent formula appears to estimate pg TEQ/g lipid. Please add text to reference the half-life and indicate the assumptions you have made regarding its use in this report.

Section 7.1, Page 68, formula for BB_o: The units of BB_o and BBB are probably TEQ pg/g as evidenced by the parenthetical value of 21.8 pg/g lipid. Please indicate TEQ here and elsewhere in the specified units for this formula or else clarify the unit for BB_o. Please cite a reference for the formula or explain how it was derived.

The use of the 1,000-fold unit correction factor for "pg/ng" is likely unnecessary (note: it does not appear that this factor has actually been used in Cantox equations).

It is also noted that this appears to the first time that the term "ABD_{acute}" is used. In our review of the report, it was somewhat confusing and hard to exactly replicate. It appears that the term "ABD_{acute}" refers to the values provided in Tables 5-12 to 5-17 (since these values represent absorbed doses) and if this is the case, it should be referenced.

It is also unclear how the term "ABD_{acute}" accounts for exposures on multiple days. For example, the Mixer/Loader under the Accident 1966 scenario was associated with a central estimate of 740 ng/kg bw (see Table 5-12). As noted earlier in our request for clarification, no time units were provided by Cantox but it would seem that the estimate was 740 ng/kg bw per day (or accidental spill event) and that an accidental spill event would occur once per day (see page 30) for the 3 days that spraying occurred. It is unclear if and how multiple spill events were considered in the calculations. Cantox should clarify this issue.

Section 7.1, Page 69, formula for $BB_{year\ 1}$: The units are probably pg TEQ/g lipid. Because Table 7-1 is derived from BBB (pg TEQ/g lipid) in the formula, the units cited in the table should be pg TEQ/g lipid. Please fix or explain. Please cite a reference for the formula or explain how it was derived.

Table 7-1, Page 69: The absorbed dose column is somewhat confusing. Specifically, in 1966, there would have been 3 days where the exposure was elevated (i.e., 3 days at 30,016 pg/kg bw/day); however, the table appears to imply that this exposure occurred for the entire year.

The values provided appear to be for routine exposures and no accident. Perhaps this could be specifically stated.

The values would change if the Lorber (2002) values were used (once again, it is not being suggested that these are more accurate but could be worthy of discussion since they are from the US EPA).

The use of significant figures may be inappropriate in some of these tables (i.e., 5 significant figures?).

Acronyms (e.g., BB) should be defined.

Tables 7-2 to 7-7: Risk calculations appear to match the data provided earlier; however, if the exposure estimates are revised based on the earlier comments, then these risk estimates will also change.

It is noted that the acute TRVs are typically only derived for evaluation of once per lifetime events. This was noted earlier by Cantox as an assumption that was reasonable (i.e., the same people did not participate in both 1966 and 1967 events).

Figures 7-1 to7-5: These figures work well for describing the Body Burden estimates but not so well for the absorbed dose rates. Issues with the absorbed dose rates include:

- the TDI is not accurately shown in the figures; and

- the dotted line seem to imply that the elevated absorbed dose rate persisted for a couple of years (as opposed to 3 days in some cases)

Similar to previous comments, acronyms (e.g., BB) should be defined and previously used terminology (e.g., TDI, Body Burden$_{TRV}$) should be continued to be used.

The arrows should be explained.

Section 7.3.1, Page 81, paragraph beginning "Tables 7-11 through 7-16…". As written, this paragraph conflicts with the fifth bullet on page 92. The paragraph is certainly less assertive than the material on page 92 and should be revised to harmonize with the eight bulleted items on pages 92 and 93.

Section 8.2, Page 90, sixth bullet: The formulas used for exposure assessment appear to have specified a fixed half-life of 7.1 years. Therefore "assumption of a linear half-life" should be changed to "assumption of a constant half-life".

Section 8.2, Page 90: As noted by Cantox, the chronic TRV for dioxin is of questionable relevance. Specifically, if it was known that only men were using the area, the potential lack of relevance of the chronic TRV could be further discussed. It should be stressed, however, that we have not been provided with any information that suggest only males were present.

The acute TRV from the ATSDR could also be further discussed. More specifically, it was based on immune suppression in mice exposed to dioxins and then challenged with the influenza virus. The potential reversibility of this effect could be discussed.

Section 8.3, Page 91, last bullet, first sentence: "pg/g lipid" should be "pg TEQ/g lipid".

Section 9.0, Page 92, first bullet, second sentence: Replace "effects would have occurred" with "effects will occur".

Section 9.0, Page 92, second bullet: Replace "may have experienced" with "may have already experienced".

Section 9.0, Pages 92 and 93: The bulleted items on these pages should be copied into the executive summary as a bottom line for the report.

References, Page 102: The Ruby et al reference should be 2002, not 2004. The citation of this reference on page 40 should be revised accordingly.

Page A-1, paragraph beginning "According to the …". This is a nice calculation, leading to the conclusion that PCP was applied as a salt rather than as water insoluble PCP. To

help the reader follow this more readily, please add the phrase "or, equivalently, 4 lb/gal" to the end of the third sentence.

Table A1-1.3, Page A-3: It is unclear how the mean values were derived. It is recommended that 2 or 3 significant figures be reported in the table.

Page A-4, paragraph beginning "In 1971, Elvidge …". Is it "Bionetics" or "Biometrics"?

Page A-10, paragraph beginning "Technical grade picloram …", last sentence" Replace "in the 200 region of 200 ppm" with "in the region of 200 ppm".

Page B-8, Table B1-3.3. The Longnecker and Michalek (2000) reference appears inappropriate because the table is intended to summarize results in exposed individuals, as represented in the Fingerhut reference. The Longnecker et al paper described diabetes in control subjects of the Air Force Health Study (those who had no occupational exposure to herbicides). A more appropriate reference would be Henriksen GL, Ketchum NS, Michalek JE and Swaby JA. Serum dioxin and diabetes mellitus in veterans of Operation Ranch Hand. *Epidemiology* 1997;8(3):252-258, which describes diabetes in the Ranch Hand sprayers and was used by the IOM to render their opinion regarding Agent Orange and diabetes.

Page B-11, Table B1-3.4, last item: Also mention spina bifida in Ranch Hand offspring. You might write, "A trend of increased risk of spina bifida in Ranch Hand offspring was found" and cite Wolfe WH, Michalek JE, Miner JC, Rahe AJ, Moore CA, Needham LL and Patterson Jr DG. Paternal serum dioxin and reproductive outcomes among veterans of Operation Ranch Hand. *Epidemiology* 1995;6:17-22.

Page B-15, paragraph beginning "In the U.S. EPA's draft …", first sentence: Replace "they have" with 'researchers".

Page B-19, paragraph beginning "Charnley and Kimbrough…", first sentence: Replace "argues that" with "argue that".

Page B-21, paragraph beginning "The U.S. EPA …": It appears inconsistent to spell out this agency and the CDC here because these were abbreviated throughout the report up to this point. We suggest maintaining the abbreviations and drop the parenthetical. Thus, drop the parenthetical and replace "Centers for Disease Control" with "CDC". For your information, and not to be used here, the official name of CDC is the Centers for Disease Control and Prevention.

Page B-22, top line: Replace "that TCDD are largely" with "that TCDD is largely". This section points out the variation in nomenclature for 2,3,7,8 tetrachlorodibenzo-p-dioxin. We think the reader should be advised of this at the front of the report. On page ii, for example, item 1, replace "(TCDD)" with "(TCDD, 2,3,7,8-TCDD, or dioxin)", because all three of these names are used throughout the report.

Page B-23, paragraph beginning "Peak exposures to TCDD…", last sentence: Replace "postualted" with "postulated". Also, to complete the thought, please extend the sentence to explain "inducible" means, we presume, by sequestration of TCDD in the liver by CYP1A2.

Page B-25, paragraph beginning "The discrepancies between…", first sentence: Replace "study among individuals" with "study in persons".

Page B-27, paragraph beginning "Anderson et al…": Insert a blank line preceding this paragraph and after this paragraph.

Page B-27, bottom of the page: This section summarizes PBPK modeling of dioxin elimination, concluding that use of a variable elimination rate that corresponds to enzyme induction provides better fits to experimental data than models that use a fixed rate of elimination. Yet, on page 68 and elsewhere, you indicate that a fixed half-life of 7.1 years was used in your calculations. We suspect that you used a fixed half-life because current exposure and risk estimation methods do not accommodate a variable elimination rate. Provide text to explain why you used a fixed half-life of 7.1 years.

Table B1-5.1, Page B-32: It appears that the units for the column "Related human EDI" should have been "ng/kg bw/day" (as opposed to "pg/kg bw/day").

Page B-34, paragraph beginning "The U.S. EPA began…", last sentence: As far as we know, Paustenbach is employed by Exponent, a consultation company for the pesticide industry. You might leave the sentence as it is, or rewrite as "Pesticide industry consultants, Paustenbach et al 2000, have pointed to …".

Page B-35, paragraph beginning "U.S. EPA (2004b)…", second sentence: Replace "$(mg/kg/day)^{-1}$" with "$(mg/kg/day)^{-1}$". The narrative in this paragraph is further complicated by a recent paper that shows an increased all-site cancer risk with dioxin in Air Force Health Study control subjects, nearly all of whom have background dioxin levels; see Pavuk M, Michalek JE, Schecter A, Ketchum NS, Akhtar FZ, Fox KA. Did TCDD Exposure or Service in Southeast Asia Increase the Risk of Cancer in Air Force Vietnam Veterans Who Did Not Spray Agent Orange? *Journal of Occupational and Environmental Medicine* 2005;47(4):335-342.

Page B-38, top of the page, second line: Replace "At the Elgin spray testing" with "At the Eglin spray testing".

Page B-49: The specification of the page numbers in the Murray et al reference (1979) incorrectly includes a square instead of a hyphen.

Page B-58, Table B2-2.1, Half Life (environmental) panel: It seems odd to express the half-life in hours given that later in this appendix it is expressed in years. Please convert hours to years.

Page B-63, paragraph beginning “Renal Effects”: Replace “HCB exposure in humans have not” with “HCB exposure have not”. Sentence beginning “Increased kidney …”, replace “≥7” with “greater than or equal to 7”.

Page B-69, paragraph beginning “Among a group of 85”, first sentence: As written this is not a sentence. A fix would be to combine this with the second sentence by replacing “and HCB. An in vitro” with “and HCB, an in vitro”.

Page B-70, paragraph beginning “HCB did not induce”, last sentence: Delete “there was”.

Page B-71, paragraph beginning ‘Infants and young children…”, sentence beginning “Breast-fed…”: Delete “also”.

Page D-5, top line. The conclusion of this commendable effort to validate the application of PHED data is understated. In fact, the results, as evidenced by skin 2,4-D levels in Table D-2, are consistent with the estimated exposure levels by receptor category described in Tables 5-12 through 5-17, indicating that the mixer/loader receptor had exposures at least an order of magnitude greater than the flagman receptor. This information should be added to the summary paragraph on page D-5.

References

Health Canada. 2004. Federal Contaminated Site Risk Assessment in Canada – Part I: Guidance on Human Health Preliminary Quantitative Risk Assessment (PQRA) and Part II: Health Canada Toxicological Reference Values (TRVs). Environmental Health Assessment Services, Safe Environments Programme, Health Canada, Ottawa, Ontario.

Lorber, M. 2002. A pharmacokinetic model for estimating exposure of Americans to dioxin-like compound in the past, present and future. Sci Tot Environ 288:81-95.

ORNL. 2006. Risk Assessment Information System (RAIS) On-Line Database. Oak Ridge National Laboratory, Oak Ridge, Tennessee. Web site: http://risk.lsd.ornl.gov/rap_hp.shtml.

Richardson, G.M. 1997. Compendium of Canadian Human Exposure Factors for Risk Assessment.

Appendix: Worked Example Calculations

The following worked examples illustrate how we have not been able to reproduce the Cantox exposure estimates. It is stressed that the values provided below do not represent exposure estimates that are considered to be more accurate than the Cantox estimates. Rather these worked examples serve to illustrate that it is not completely intuitive how Cantox estimated the exposure. Comments from Cantox should be sought before assuming that the Cantox estimates contained errors.

Example #1: 1966 Mixer/Loader Accident Scenario – Dermal Exposure to PCDD (High Estimate)

As provided on page 30 of the report, the following equation was used to estimate exposure:

$$EXP_{Accidental} = \frac{S \times AC \times CF \times SAR \times P}{BW}$$

S = spill amount (0.5 L/day)
AC = concentration (g/L) – this is difficult to determine which value Cantox recommended for use. For PCDD, a maximum value of 45 ppm was previously noted but it was unclear if this was 45 mg/L or 45 mg/kg (see pages 6 and 24). For this worked example, 45 ppm was assumed to be 45 mg/kg which when adjusted for a density of 1.8 g/mL is 81 mg/L or 0.081 g/L (note that density is not provided in the document).
CF = conversion factor (1,000 mg/g)
SAR = 0.44 (as provided on page 30)
P = proportion absorbed. For PCDD, Table 5-9 on page 34 provided an upper value of 0.029 which was assumed for this worked example
BW = body weight (70.7 kg) (see Table 5-9)

Based on the above, the exposure was estimated as:

$$EXP_{Accidental} = \frac{0.5 \text{ L/day} \times 0.081 \text{ g/L} \times 1{,}000 \text{ mg/g} \times 0.44 \times 0.029}{70.7 \text{ kg}}$$

$$= 7.3 \times 10^{-3} \text{ mg/kg bw/day}$$

$$= 7{,}300 \text{ ng/kg bw/day}$$

Thus, the exposure was estimated to be 7,300 ng/kg bw/day (for 3 days) while Cantox (see Table 5-12, page 41) estimated the exposure to be 5,100 ng/kg bw/day.

Worked Example #2: 1966 Mixer/Loader Accident Scenario – Dermal Exposure to Hexachlorobenzene (Central Estimate)

As provided on page 30 of the report, the following equation was used to estimate exposure:

$$EXP_{Accidental} = \frac{S \times AC \times CF \times SAR \times P}{BW}$$

S = spill amount (0.5 L/day)
AC = concentration (g/L) – this is difficult to determine which value Cantox recommended for use. For hexachlorobenzene, a central value of 200 ppm was previously noted but it was unclear if this was 200 mg/L or 200 mg/kg (see page 6 and 24). For this worked example, 200 ppm was assumed to be 200 mg/kg and when a density of 1.8 g/L was assumed this was estimated to be 0.36 g/L (once again, density is not provided in the report).
CF = conversion factor (1,000 mg/g)
SAR = 0.44 (as provided on page 30)
P = proportion absorbed. For hexachlorobenzene, Table 5-9 on page 34 provided an upper value of 0.005, which was assumed for this worked example
BW = body weight (70.7 kg) (see Table 5-9)

Based on the above, the exposure was estimated as:

$$EXP_{Accidental} = \frac{0.5 \text{ L/day} \times 0.36 \text{ g/L} \times 1{,}000 \text{ mg/g} \times 0.44 \times 0.005}{70.7 \text{ kg}}$$

$$= 5.6 \times 10^{-3} \text{ mg/kg bw/day}$$

$$= 5{,}600 \text{ ng/kg bw/day}$$

Thus, the exposure (as a central estimate) was estimated to be 5,600 ng/kg bw/day (for 3 days) while Cantox (see Table 5-12, page 41) estimated the exposure to be 394 ng/kg bw/day.

Worked Example #3: 1967 Mixer/Loader Routine Scenario – Dermal Exposure to PCDD (Upper Estimate)

As provided on page 29 of the report, the following equation was used to estimate exposure:

$$EXP_{Dermal\ Routine} = \frac{AR \times AT \times UE_{Dermal} \times P}{BW}$$

AR = application rate – this is difficult to determine which value Cantox recommended for use. The highest application rate reported in Table 5-4 (page 28) is 9.1×10^{-6} g/m^2 which according to the conversion factor on page 26 is equal to 1.0×10^{-6} lbs/acre
AT = area treated – this is difficult to determine which value Cantox recommended for use. On page 5, it seems that 12 plots per day and 3 acres per plot results in 36 acres per day is reasonable
UE_{Dermal} = Dermal unit exposure - 2.86 mg/lb (as provided in Table 5-6)
P = proportion absorbed. For PCDD, Table 5-9 on page 34 provided an upper value of 0.029 which was assumed for this worked example
BW = body weight (70.7 kg) (see Table 5-9)

Based on the above, the exposure was estimated as:

$$EXP_{Dermal\ Routine} = \frac{1.0 \times 10^{-6}\ \text{lb/acre} \times 36\ \text{acres/day} \times 2.86\ \text{mg/lb} \times 0.029}{70.7\ \text{kg}}$$

$$= 4.2 \times 10^{-8}\ \text{mg/kg bw/day}$$

$$= 0.042\ \text{ng/kg bw/day}$$

Thus, the exposure (as an upper estimate) was estimated to be 0.042 ng/kg bw/day while Cantox (see Table 5-12, page 41) estimated the exposure to be 0.77 ng/kg bw/day.

Worked Example #4: 1967 Field Scout Routine Scenario – Dermal Exposure to PCDD (Upper Estimate)

As provided on page 36 of the report, the following equation was used to estimate the dislodgeable residue was estimated as:

Dr = Application Rate ($\mu g/cm^2$) x 0.1

The Application Rate was not specifically referenced by Cantox in the equation but the highest application rate reported in Table 5-4 (page 28) is 9.1 x 10^{-6} g/m^2 which is equal to 9.1 x 10^{-4} $\mu g/cm^2$. Consequently, Dr was estimated to be 9.1 x 10^{-5} $\mu g/cm^2$.

The following equation was then used to chemical transfer rate from vegetation to skin:

$$Tr = 10^{(1.09 \times \log [Dr] + 0.05)} \times 1/1000$$

$$= 10^{(1.09 \times -4.04 + 0.05)} \times 1/1000$$

$$= 10^{-4.35} \times 0.001 = 4.5 \times 10^{-8} \text{ mg/cm}^2\text{/hr}$$

$$EXP_{\text{Dermal Routine}} = \frac{Tr \times Tc \times ESA \times P}{BW}$$

Tr = 4.5 x 10^{-8} mg/cm^2/hr
Tc = contact time (assumed to be 18 min/plot x 39 plots/day = 702 minutes = 11.7 hours) (see Table 5-10, page 37)
ESA = 9,110 cm^2/day (see Table 5-10, page 37)
P = proportion absorbed. For PCDD, Table 5-9 on page 34 provided an upper value of 0.029 which was assumed for this worked example
BW = body weight (70.7 kg) (see Table 5-9)

Based on the above, the exposure was estimated as:

$$EXP_{\text{Dermal Routine}} = \frac{4.5 \times 10^{-8} \text{ mg/cm}^2\text{/hr} \times 11.7 \text{ hr/day} \times 9{,}110 \text{ cm}^2 \times 0.029}{70.7 \text{ kg}}$$

$$= 2.0 \times 10^{-6} \text{ mg/kg bw/day}$$

$$= 2 \text{ ng/kg bw/day}$$

Thus, the exposure (as an upper estimate) was estimated to be 2 ng/kg bw/day while Cantox (see Table 5-16, page 43) estimated the exposure to be 0.030 ng/kg bw/day.

Worked Example #5: 1966 Mixer/Loader Routine Plus Accident Scenario – Predicted Body Burdens (Central Estimate)

As provided on page 68 of the report, the following equation was used to estimate the body burden (note: the 1,000-fold "pg/ng" has not been included in the equation, as it appears to be a typo that was not carried into Cantox equations):

$$BB_0 = BBB + (ABD_{acute} \times 4.04)$$

BBB = 21.8 pg/g
ABD_{acute} = 740 ng/kg bw = 740 pg/g bw (see Table 5-12)

$$BB_0 = 21.8 \text{ pg/g} + (740 \text{ pg/g} \times 4.04)$$
$$= 3{,}011 \text{ pg/g lipid}$$

Thus, the Body Burden estimate on Day 1 of 3,011 pg/g lipid matches quite closely the value of 3,022 pg/g lipid estimated by Cantox (see Table 7-9; page 75). However, it does not appear that a spill event occurring once per day for 3 days is considered in the approach. In addition, previous comments on our lack of confirmation of the exposure estimates in Table 5-12 may affect the body burden estimate.

After 1 year, the Body Burden was estimated as:

$$BB_1 = BBB + (BB_0 e^{-kt})$$

BBB = 21.8 pg/g lipid
BB_0 = 3,011 pg/g lipid
k = 0.693/7.1 years = 0.098 yr^{-1}
t = 1 year

$$BB_1 = 21.8 \text{ pg/g lipid} + (3{,}011 \text{ pg/g lipid} \times e^{-0.098})$$
$$= 21.8 \text{ pg/g lipid} + (3{,}011 \text{ pg/g lipid} \times 0.907)$$
$$= 21.8 \text{ pg/g lipid} + 2730 \text{ pg/g lipid}$$

Thus, the Body Burden estimate after 1 year of 2,752 pg/g lipid matches quite closely the value of 2,744 pg/g lipid estimated by Cantox (see Table 7-9; page 75).

HEALTH CANADA COMMENTS
TASK 3A-1 TIER 1 DRAFT RISK ASSESSMENT REPORT

General Comments

- "TCDD", "PCDD" and "PCDF" appear to be used inconsistently throughout the report.
  - When "TCDD" is used, it is unclear whether the term is inclusive only of 2,3,7,8 TCDD, all TCDDs, or of all dioxins and furans. This is particularly important when discussing the concentration of contaminants in the herbicide products and when discussing the toxicity of dioxins and furans. Throughout the report (e.g. Section ES-2.0), when contaminants are reported, it is unclear if the report is referring to only TCDD, or TEQs that would consider all congeners.
  - Throughout the main report and in the appendices, units used to report levels of mixtures of dioxins and dioxin-like substances are not consistent (e.g. in environmental media, doses, body burdens. This makes it difficult for the reader to authenticate or compare reported concentrations and involved calculations. Units are most often reported just as pg/.... or as pg TEQ/... regardless of which toxic equivalency factors scheme was used. For example, levels of PCDD/DFs in Table C1-1.10 (page C-8) should have been reported as I-TEQ pg/kd bw/day for the "historical EDIs" and as TEQ-WHO_{98} pg/kd bw/day for the "current EDIs" instead of "pg/kg bw/day."
  - The entire document needs to be carefully reviewed to ensure clarity and as much consistency as possible.

- It would be useful to present information regarding the definition of dioxins and dioxin-like substances "up front", in a stand alone section that can be easily referred too by the reader. (In the present document, there is a only very brief description in Appendix B.) This section could comprise the following elements:
  1) A definition of the classes of dioxin-like substances
  2) A concise summary of how and why Toxic Equivalency Factor schemes were created and how the calculations are done.
  3) A clear description of the nomenclature of the various schemes presented in US EPA (2003). For example:
     I-TEQ: denotes the NATO International TEF scheme.
     TEQ-WHO94:.....
     TEQ-WHO98.....
  4) A comparison table illustrating the differences between schemes and

  The contractor could consider adopting the complete US EPA (2003) nomenclature with the subscripts D, F and P such as "TEQDF-WHO98"

- Throughout the report, exposure and risk estimates are characterised using different and inconsistent terms such as "central, low and high" estimates, "realistic, yet conservative" estimates, "upper-case estimates", etc..
  - It would be helpful to use consistent terminology throughout the report.
  - As these terms are subjective and difficult to interpret, it would be helpful to clearly document and reference the basis for each assumption in each estimate and to characterize the inherent uncertainty and/or conservatism. Where the

basis is simply "expert opinion", this should be noted.

- It could be helpful to include a general discussion of uncertainty and conservatism. For example, could explain that conservative assumptions are applied when there is high degree of uncertainty around a parameter. To help put the assessments in context, the impact of multiplying a series of high end assumptions should be clearly explained (i.e. it exponentially compounds the conservatism and can result in very exaggerated exposure\risk estimates).
- A summary table of the assumptions used for each estimate, and the conservatism and uncertainties, would help the reader interpret the "central, low and high" risk results in proper context.
- Accident scenarios should be clearly differentiated from routine events (e.g the difference between the spills and plashes inherent to mixing /loading activities that are captured in the PHED estimates, and truly accidental major spills). .

• Throughout the report, there are inconsistencies between the problem formulation and the actual receptors/exposure pathways for each receptor assessed.
  - Details are provided in comments specific to each section of the report (below).

• Some the equations, data and calculations presented in the report are difficult to verify and/or reconcile.
  - For some equations, the units do not cancel out (details below).
  - Input parameters for the equations are sometimes difficult to locate - e.g.,some are only in the appendices.
  - It would be very useful to include at least one "sample" calculation for each component of the exposure and hazard quotient calculations, to help the reader follow through the calculation logic. In addition, it would be helpful to include the equations used and inputs for the equations, including the toxicity reference values, in the footnotes for each tables.

• The document would be easier to read if:

I
  - Information was readily available in the relevant text sections - for example, while the derivation of the dermal absorption values are discussed in the main report, the actual values are difficult to locate, other than is the appendices.
  - A glossary of technical terms, including a list of all acronyms was included and . each acronym was clearly defined the first time it is used.
  - Equations were numbered for easy cross reference.

<u>Plain Language Executive Summary</u>

• The Plain Language Executive Summary needs to be written insimpler, less technical language, in order to be easily understood by a layperson.
  - Section ES-3.0 should include a summary of the key aspects of risk assessment methodology, including basic concepts such as: RISK = EXPOSURE x TOXICITY. Other specific examples are provided below.

• The glossary (see comments above) should include terms such as "defoliants,"

"herbicides," "receptor" and "conservative assumptions." In addition, each technical term or acronym should be explained the first time it is used.

ES-1.0: Introduction

- Suggest edit to first paragraph sentences 2 and 3 to clarify that herbicides as well as their contaminants will be evaluated in subsequent Tiers. Suggested edit is:
  "As part of this commitment, the Government of Canada has engaged non-governmental experts to assess the possibility of military and civilian personnel exposure to herbicides and contaminants within these herbicides, the potential herbicide and contaminant dose received by these personnel and the potential of these herbicides and contaminants to cause harm. The following report documents the human health risk assessment, which was used to estimate potential exposures, characterize potential health risks, and determine, in an objective manner, whether exposures to herbicides and associated contaminants used at CFB Gagetown may be associated with potential human health risks."
- Second paragraph: The report and the statement of work for this contract indicates a risk assessment is to be conducted for herbicide use from 1952 to the present. However, the description of the tiers indicates that herbicide use from 1956 will be considered. This should be corrected or a rationale provided as to why 1952 to 1955 need not be assessed.
  .

ES-2.0: Description of Tier 1

- Define "CO"

ES-3.0: Health Risk Assessment methodology

- The report states *"A non-measurable or very low risk is considered 'acceptable'..... Health Canada assumes that the development of an additional cancer in one person out of 100,000 people... is acceptable.*" The word "acceptable" should be changed: The guidance for conducting preliminary quantitative risk assessments (PQRA)) does not specify an acceptable risk for carcinogens, but rather qualifies a risk range of 1 cancer in 100,000 as "de minimus' or "essentially negligible". Generally, Health Canada views 1 cancer in 100,000 to 1 cancer in 1,000,000 as a minimally desirable targets, depending on the specific situation and on the degree of conservatism and uncertainty in the risk assessment.

ES-4.0: Problem Formulation

- First bullet, Mixer/Loader/Applicator:
  - Does not state that accidents will be considered for this receptor, yet in ES-7.0, "mixer/loader accident" scenario is cited as resulting in elevated risks. Consider the above comment on need to clearly delineate accident scenarios from routine work scenarios.
  - Text states *"It was assumed that a single person was responsible for all three activities".* It is unclear what this assumption is based on; please cite references. Similar assessments by pesticide regulatory agencies such as the U.S. Environmental Protection Agency (EPA) do not assume the pilot and mixer/loader to be the same person, as the pilot requires a special licence to operate aircraft, which most mixers/loaders usually do not have. Technical

Memorandum 141 (Demaree and Creager 1968) states that one pilot applied all mixtures in about 30 hours of actual flying time over three consecutive days (but does not identify the number of personnel involved in mixing and loading, or the number of flagmen). Since there was only one pilot, would he have had time to also do all the mixing/loading?

- Second bullet, Flagger:
  - Ingestion is identified as an exposure pathway here, but was not the Problem Formulation (section 4-1) nor assessed in the exposure assessment. Regulatory agencies generally do not consider ingestion to be a typical exposure pathway for flaggers.
- Third bullet, Post-application Scouts:
  - The text states *"It was assumed that individuals acting as flaggers also may be the post-application scouts"*. Please discuss and reference the basis for this assumption. Similar assessments by pesticide regulatory agencies such as the U.S. Environmental Protection Agency (EPA) do not assume that the scout and flagger are the same person. Scouting is usually conducted to determine efficacy of the application. Considerations could include: Would the efficacy of a defoliant be apparent immediately after the application (as suggested by the assumption that flaggers also scout)? Would flaggers have the specific expertise that scouts require to assess efficacy? .
- Fourth bullet, On-Site Military Trainee:
  - Clarification of the types of activities conducted by this receptor, and the assumed time frames (post application) for the assessment for this receptor, is required. (See specific comments below)
- There are some possible exposure groups are not addressed in the report. It is important to either assess theses group, or to conclusively determine that these activities did not occur (at least for the Tier 1 assessment scenarios), given the concerns of individuals who believe they may have been exposed in these ways:
  - Brush clearers and brush burners. A large number of individuals believe they may have engaged in this potentially relatively high exposure activity.
  - Family members or others who may have had contact with "contaminated" clothing that personnel brought home.

ES-5.0: Exposure Assessment

- Please clarify the sentence "A range of exposures to people at CFB Gagetown in 1966-67 was estimated."
- Section refers to "high, low and central estimates". Later, new terms such s "upper-case estimate" and "worst-case scenario" are used. Later in the report (p. 35), the estimates are called "upper, lower and central approximations." See general comments (above) on the importance of consistent terminology and constructive suggestions.
- Terms used are rather technical for a plain-language summary. For example, instead of "worst-case parameter values" could say "worst-case assumptions". "
- Worst-case scenario" should be defined (in terms of the intention to overestimate the risk).

ES-6.0: Hazard Assessment

- Table ES-1:

- The non-cancer health effects for dioxins should conclude with *"...and other developmental effects"*.
- The cancer effects associated with dioxins have not only been linked with occupational exposures, but also in situations where the general population has been exposed though industrial accidents (e.g., Seveso). Reference should be made to such situations.

• The diseases listed should be defined for the lay public.

ES-7.0: Risk Characterisation

• First paragraph:
- This text in paragraph appears to state that exposure = risk. For example, . *"Military trainees were assumed to have long term exposure and therefore long term risks"*. Text should be clarified to avoid propagating this common misconception and to be consistent with the bullets that follow.

• Dioxins, 2nd bullet:
- Sentence is not clear and reference to "acceptable" should be removed (per comment above). It would be better to rephrase sentence as, *" Long term cancer (and other ??) risks were concluded to be negligible for military trainees experiencing long-term exposure."*

• Dioxins, 3rd bullet:
- Does this statement really mean that risks were elevated for >50 years or does it mean that body burdens were elevated for >50 years? It would be useful to provide more characterisation of the relationship between body burden (exposure) and risk, including more specificity on specific risks and on strength of the association between the estimated body burden and the risk.
- Clarify what is meant by "spray accident scenarios"

• HCB, general:
- Terminology may be too technical and in some cases is poorly defined or too subjective: e.g : *"minor exceedances", "marginal exceedance" and "highly conservative"*. This is the first time the word *"conservative"* is used. The word should be defined, including a plain language explanation of what leads to conservatism in risk assessment.
- Should note that three risk estimates were made (high, low and central) and clarify whether the conclusions drawn are based on the "central" estimate, or all the estimates.

• HCB, 1st bullet:
- The conclusion that "overt signs of toxicity" would be the result of "active herbicide ingredients" is not substantiated by the risk assessment in this report. Conclusions should be made only after the risk assessment for the active ingredients has been conducted (which will be in the later tiers).

• HCB, 2nd bullet:
- It would be better to rephrase sentence as, *" Long term cancer (and other ??) risks were concluded to be essentially negligible for military trainees experiencing long-term exposure."*

ES-8.0: Uncertainties

- The sentence related to what risk managers need is irrelevant for the plain language summary and should be removed.
- The Plain Language Summary (and the report in general) is for a public audience, who needs help to understand the uncertainties in the risk estimates. This section states that over-predicting is preferred to under-predicting, but does not give any indication of factors or areas in which under-prediction is possible. A more complete and systematic discussion of uncertainty could include a table of the various factors in the risk assessment and a corresponding statement about whether the data uncertainties are likely to lead to over-prediction or under-prediction, and how this was addressed, e.g., use of uncertainty factors, etc. (see General Comments above)

Section 1.0 Introduction:

- Footnote 1, page 1:
  - To avoid confusion, consistent terminology should be used throughout the document. Here it is specified that PCDDs and dioxins refer to PCDDs, PCDFs and dioxin-like PCBs, yet elsewhere in the document, PCDFs are used with PCDDs; does that mean that dioxin-like PCBs are excluded? It would be better to use either use dioxins or PCDDs, not both, to represent the same term. See general comments for additional suggestions.
- Page 2:
  - Text states *"There is a need to examine the potential for exposure before any risk can be determined."* It is unclear why there is a need - suggest explaining the implicit point here, that if there is no exposure, then there is no risk.
  - It is noted in the report and the statement of work for this contract that a risk assessment is to be conducted for herbicide use from 1952 to the present day. However, the description of the tiers indicates that herbicide use from 1956 will be considered. A rationale as to why 1952 to 1955 will not be considered needs to be provided.

Section 2.0 Description of Tier 1:

- Page 3, 1st paragraph
  - References to Demaree and Creager, 1968 – references section has 1968a.
  - Text states: *"This is an important point since it suggests that data regarding important factors such as rates of application and deposition that have been developed for exposure models used for Vietnam...should be comparable for the experimental applications of herbicide at CFB Gagetown."* This statement needs to be substantiated further. It is unclear if the report authors actually compared the rates used at CFB Gagetown to those used in Vietnam. Various rates are used to assess the efficacy of a product as compared to actual use conditions that may have been used in Vietnam.
- Page 3, 2nd paragraph:
  - *"The tests occurred over a two year period."* This statement could be clarified to indicate the small number of days during which testing occurred in the two-year period.

- Figure 2-1:
  - In title: replace "or" with "and", to read *"Application for 1966 (shown in blue) and for 1967 (shown in green)"*. Also define what the red-outlined area is.
- Page 4, 1st paragraph:
  - Define the abbreviation "CO"
- Page 4, 4th paragraph:
  - Text read *".....each plot received a series of four passes...."*. This contradicts the assumption used in the spray drift report where a single spray line with a 100 feet spray swath was assumed, as the report did not specify. Please clarify the discrepancy.
- Page 5:
  - Reference to Demaree and Hawes, 1968 - references section says 1968b.
  - The phrase "*contaminants of concern*" is elsewhere in report stated as "*chemicals of concern"*. Again, it would be helpful to maintain consistent terminology throughout the report.
- Page 5, Bullet 1:
  - Text states that TCDD is present in 2,4,5-T. It is unclear if this implies that only TCDD is present and other dioxin and furan congeners are not. Please clarify.
  - Text reads *"At the time of application, there was no discernible contamination of 2,4-D by PCDDs or PCDFs."* This suggests that 2.4-D samples were analysed for PCDDs and PCDFs and none were detected. Does the statement actually mean that there was limited information on the levels of PCDDs and PCDFs in registered 2.4-D? Please clarify the basis for concluding that all the dioxin agents orange and purple arose only from the 2,4,5-T.
- Page 5/6, including and Tables 2-1 and 2-2:
  - Please provide references for reported concentrations of contaminants in Agent Purple and Agent Orange and document reasons where assumptions/conclusions differ from those of Jaques Whitford.
  - Please be careful to differentiate between unregistered agent products and registered herbicides that contained 2,4,5-T.
  - Please consistently specify whether only TCDD was measured, or all dioxin and furan congeners. If only TCDD was measured, specify whether there is the likelihood that other congeners would be present and the implications for the total TEQ and the risk assessment.
  - It would be cleared to label the last column "<u>Assumed</u> Contaminant Concentration" to indicate these are assumed and not measured or known values.
  - Please be consistent about whether contaminant concentrations are expressed as TEQs and reference the source of the TEQs for the calculation.
  - Please add a footnote referencing where the estimate of HCB in picloram came from (not explained in report).
  - Ist footnote - what does the last sentence mean - are words missing?
  - It is unclear why there are there footnotes for Agent White and Agent Blue when these chemicals are not mentioned anywhere else in the report.
  - Last row in Table 2-2 refers to "focus contaminants". Please define this term.
  - In the published literature, HCB is identified as a contaminant of PCP and should be assessed as such. See comments for Appendix A.

Section 3.0 Health Risk Assessment Methodology:

- Section 3.1, Problem Formulation:
  - Text reads *"...takes into account chemical-specific parameters, such as solubility and volatility..."* It as unclear how the identification of exposure pathways took such properties into account, or why these two particular properties and not mobility and persistence (generally recognized as more important determinants of fate/transport) were selected..
- Section 3.3.1 - 3rd paragraph:
  - When discussing "adverse effects," please specify "adverse health effects." Also, please introduce/explain the term, Tolerable Daily Intake.
- Section 3.4.1, page 11:
  - Please refer to comments about "acceptable" cancer risk above under section ES-3.0.
- Section 3.4.2:
  - Please provide references for the body burden approach, introduced here as "an accepted and well documented approach"
- Page 12, last paragraph:
  - Please provide rationales for why certain assumptions were used for the HCB risk assessment. Specifically, *"for chronic exposures/chronic risks, HQ and ILCR estimates have been provided for HCB, assuming annualized exposures over a maximum three year period"* and *"for the purpose of this evaluation, a duration of exposure of one year has been assumed."*

Section 4.0 - Problem Formulation:

- Section 4.1, page 13:
  - Subheading title: Contaminants of Concerns (COCs) - note that earlier, in Section 3.3.1, COC was defined as Chemical of Concern. In Section 5.3.2 they are called "contaminants of interest." In Table 2-2 they are called "focus contaminants." Please define and use one term consistently.
  - 1st paragraph: "PCDD/PCDF." Does this term include dioxin-like PCBs as per the footnote in Section 1? See General Comments for further suggestions.
  - 3rd paragraph. Text reads *"... the development of time-dependent EPC data for all environmental media would require a significant amount of historical spray application data and environmental fate and transport modeling."* This statement is vague and leaves the reader wondering, if it is feasible, possible or necessary to do this type of modelling.
  - Last sentence in Sec. 4.1: *"EPCs are further characterized in Section 4.0."* Should this be Section 5.0, as the statement is already in Section 4.0?
- Section 4.2, page 13:
  - Text reads *"The following is a preliminary list of receptor groups..."* It is unclear why this list is preliminary.
- Section 4.2, page 13. Mixer/Loader/Applicator :
  - Text reads *"A conservative approach may be taken in which it is assumed that a single person was responsible for all three activities."* The basis for this

assumption is unclear. Similar assessments conducted by regulatory agencies such as U.S. Environmental Protection Agency (EPA) do not assume that the pilot and mixer/loader are the same person. Considerations could include that the pilot requires a special licence to operate aircraft, which mixers/loaders usually do not have. It might also be useful to consider Technical Memorandum 141, which identifies that in 1968 one pilot applied all mixtures in about 30 hours of actual flying time over the three consecutive days, but does not identify the number of personnel involved in mixing and loading, or the number of flagmen. Would one pilot have had time to also do all the mixing/loading?

- Section 4.2, page 14. Flagger:
  - If it is assumed that the flagger and post-application scouting receptor were the same person, this should be noted here. However, the basis for such an assumption should be clearly documented. Similar assessments conducted by pesticide regulatory such as the U.S. Environmental Protection Agency (EPA) so not assume the scout and flagger are the same person. Scouting is usually conducted to determine efficacy of the application. Would the efficacy of a defoliant be apparent immediately after the application as suggested by the assumption that flaggers also scout? Scouts have specific expertise to assess efficacy. Is it reasonable to assume that flaggers have this expertise?
- Section 4.2, page 14. On-site Military Trainees:
  - A clearer description of the types of activities that military trainees typically do, and upon which the assessment is based, should be included. The time frames (post application) of the assessment for these receptors should be clarified and justified.
- Section 4.2, page 14.
  - Brush clearing and/or burning is an exposure activity that needs to be considered as there have been persistent statements that students and others engaged in this potentially relatively high exposure activity. Alternatively, it could be definitively determined that these activities did not occur in association with the Tier 1 spraying activities.
  - Some individuals have said that they had frequent contact with clothing contaminated with the herbicides used in the applications and which the personnel brought home. This exposure scenario should be addressed.
- Section 4.2, page 14. Off-Site Civilians:
  - The report states *"These individuals are those who may live near the military base and occasionally use specific areas of the base for recreational purposes.....would come into contact with various environmental media (e.g., soil, dust, local produce, etc.).....(i.e., spray drift depositing on nearby off-site residential properties)....This receptor group was not considered for the 1966-67 scenario as these spray areas are fairly small and remote resulting in limited opportunities for exposures. The 1966-67 spray areas will considered as part of the evaluation of this receptor group during Tiers 2 and 3 exposure scenarios."* While, it may be reasonable to conclude that off-site civilian exposure was minimal for this Tier, it is necessary to specifically address this receptor group to substantiate such a conclusion. Consideration of this group was included in the Draft Problem Formulation for this tier originally submitted to the Technical Authority.

- Some scenarios could be addressed by a relative comparison to quantitatively assessed receptors. For example, it might be argued that off-site civilians, and those walking or hunting on the base, would receive a much smaller dose than that received by flaggers and a smaller dose than other personnel in the direct vicinity of the application site during or after application (post-application scouts, on-site military trainees, etc).
- The spray drift report (Task 2D) for this tier includes information on the estimated fraction of the application rate deposited downwind of the sprayline. These estimates can be considered conservative as the contractor for Task 2D has indicated that they were based on "some worst case assumptions". Since the area sprayed is remote and small, this information could be used to estimate how far away the "safe zone" is. If deposit may be considered negligible at a specified distance from the flight line (e.g. 500 ft), it might be possible to conclude that is very unlikely that there is spray drift depositing on off-site areas that civilians access..
- The Task 2E scoping report includes relevant information to use in considering potential exposure from surface water and groundwater.
- For surface water: A possible approach would be to consider the distance to the nearest potential s.w. receptors. For example: Significant s.w. receptors identified in the 2E scoping report were those with known recreational uses, including several lakes and the Nerepis River. The 2E report maps these watersheds in comparison to herbicide application areas. Fig. 4 shows that the 66 spray area does not intersect any of the identified watersheds. The 67 spray area does lie within the watershed that drains to the Nerepis River; however, the 67 spray area is ~5 km from the main channel of the river. It may be possible to draw qualitative conclusions about the likelihood of s.w. impact given the watershed mapping, distance, time duration of applications, phys/chem properties of HCB/dioxins, etc.
- If there is in fact a surface water body within the deposition zone, it may be possible to consider s.w. receptors through a semi-quantitative assessment, incorporating reasonable high-end assumptions about deposition, flow rates, sediment binding, etc. that would to ensure that the risk assessments for any occasional ingestion & dermal contact during the short duration before the chemical is flushed out of the stream (or binds to the sediments) is protective.
- For groundwater: A possible approach could consider the presence/absence of potential historical groundwater receptors (wells) in the vicinity of the 66/67 spray area as identified in Task 2E. CFB Gagetown personnel have stated that the base bivouac wells were installed in the mid-1990s and the only well in the vicinity existing perhaps back as far as the 1960s is at Blissville. Cantox may wish to independently confirm this information with DND. Cantox could consider the range of estimated groundwater travel times provided in the 2E scoping report. This range is conservative, e.g. , without considering effects of adsorption (which would result in longer travel times). The effects of adsorption on groundwater velocity could be considered by using the simple equation for calculating a retardation coefficient based on Koc, aquifer porosity, and bulk density. Cantox could use the JW scoping report map of the potentiometric surface (Fig. 3) to visually estimate the general direction of regional groundwater

flow in vicinity of 66/67 spray areas. For any potential receptors identified (e.g., the Blissville well) that are generally down-gradient of the 66 or 67 application areas, could compare a conservative estimate of the groundwater travel-time to the time period of exposure used in the Tier 1 assessment. Regardless of the qualitative analysis, it is noted that DND personnel have stated that base wells were not used for drinking water, with the exception of Camp Petersville (as noted by Sheldon Downe in his comments on the 2E report). As Cantox proceeds with work on further tiers, Cantox may wish to independently confirm this information, and accordingly decide what g.w. exposure assumptions to make (no g.w. ingestion; very occasional g.w. ingestion; seasonal g.w. ingestion during training, etc.). The HC Technical Authority for the 2E scoping report is available to answer any questions Cantox may have about the report and the data used.

- The spray drift report (Task 2D) and the water migration scoping study (Task 2E) should be included as appendices to the Task 3a-1 Tier 1 report.

• Section 4.3, "Operable Exposure Pathways"
  - Please define what is meant by "Operable".
  - The term "realistic, yet conservative" is hard to understand. It would be better to clearly describe and characterise the uncertainties and conservatism that underlies the estimates. Please see general comments above for further guidance. .
  - Text reads *"From this, more detailed exposure pathways can be developed."* Suggest replacing "can be" with "were".
  - Please provide justification as to why some exposure pathway/ receptor combinations were screened out of further consideration (the ones noted with X's)
• Section 4.3, Figure 4-1
  - Indicate in title that this conceptual model is for Tier 1 (66/67 spray trial areas).
  - The exposure pathways and receptors in the figure are inconsistent with the pathways actually considered in the risk assessment. For example, the checks indicate that incidental ingestion from dermal contact with the herbicide product will be considered for the mixer/loader, flagger and scout; however, it appears that this was not a pathway considered in the exposure assessment.
  - Add a footnote clarifying that X means pathway not considered, while a check means the pathway is considered. Alternately, "yes" and "no" could be used.
  - Under the military trainee/trainer, indicate the meaning of the checks in parenthesis.
  - All potential pathways shown on the diagram should be discussed, even if not designated for further analysis. For example: volatilization to outdoor air is shown on the diagram, but not mentioned anywhere in the report. It was unclear why this pathway eliminated from detailed consideration. Justifications should be provided.
  - Surface water should be addressed either qualitatively or quantitatively (dermal exposure and/or ingestion). See detailed comments above.
  - Groundwater should also be addressed, at least in terms of discussing whether there were any receptors (wells) in the vicinity that were used for potable supply during the exposure period of interest). See detailed comments above.
  - Dermal contact with foliage should be addressed for all relevant receptor groups (i.e., all post application exposures). For scenarios where sufficient time has

passed for dislodgeable foliar residues to decline to insignificant levels, a qualitative discussion may suffice).

- Last column heading includes military "trainer" as does last footnote. "Trainer" not mentioned anywhere else in report.
- "Applicator" is not included as a receptor in the figure, yet it is considered throughout the report. -

• Section 4.3.1.1
  - Text reads *"...employed the use of exposure data provided by the Pesticide Management Regulatory Agency, literature-based values, as well as a number of conservative assumptions."* This wording suggests that the first 2 sources (PMRA and literature) are not necessarily conservative. Please clarify whether the PHED is considered to be conservative or realistic (and provide references/justification for the conclusion). Were literature-based values used in a conservative manner? Please provide some clarification on the above statement .
  - "Pesticide Management Regulatory Agency" should be "Pest Management Regulatory Agency"
  - Text read *"Dermal and inhalation exposure data for the mixer/loader/applicator scenario can be estimated using predicted loading values from the Pesticide Handlers Exposure Database (PHED) (PMRA 2002)."* Consider deleting "PMRA 2002" and adding *" PHED model runs for various scenarios were provided by PMRA"*
  - A general description of the types of studies in the PHED database would be useful. It would help characterise the risk assessment to clearly note that the studies in PHED asses exposure under typical conditions, which includes typical spills and splashes during open mixing and loading activities, and the type of direct overhead exposure that would occur during actual flagging activities. It could also be noted that some of the flagger data in PHED is from studies of agricultural applications which may overestimate exposures for forestry flaggers as there is no canopy effect during agricultural applications.
  - Remove the second "generic" form the sentence beginning *"PHED provides generic passive dosimetry data for ~~generic~~ mixer/loader/applicator exposure....."*
  - Please clarify what is meant (in the context of PHED subsets) by "These focussed on the fact that relatively small amounts of each pesticide formulations were prepared, but multiple combinations or dilutions were applied from a helicopter delivery system"
• Section 4.3.1.1, page 18:
  - Please provide references for the protection factor of coveralls and chemical-resistant coveralls. (e.g. US EPA)
  - 2nd paragraph, 1st sentence: *"Failure to....."* is not a complete sentence.
  - 2nd paragraph: Text reads *"This may include the use of dermal loading data for clothing scenarios "a" to "c" as listed above which are more representative of individuals wearing casual clothing rather than clothing typically worn for handling herbicides."* Clothing scenario "a" was short pants, short sleeves and no gloves, but this scenario was not used in any of the exposure assessment scenarios. Is this clothing scenario really considered likely?
• Section 4.3.1.1, page 18, Formulation Type:

- Text reads *"Predicting exposures during the mixing and loading stages will be heavily influenced by the herbicide formulation type."* Replace "will be influenced by" with "is dependent on."

- Section 4.3.1.2, Page 19: Flagger/Post Application Scout
  - 1st paragraph: Reference is made to incidental ingestion for flagger and post-application scout; however, this pathway was not considered in the exposure assessment.
  - 3rd paragraph: Please justify assumption that flagger and post-application scout would be the same person and characterise the degree of conservatism associated with that assumption.
  - 3rd paragraph: The exposure pathways described for post-application scouting are not consistent with Figure 4-1 or with the exposure assessment conducted for this receptor. These pathways are *"dermal contact with impacted soils.....inhalation of re-suspended dusts, incidental ingestion of soil or dusts, or inhalation of smoke containing COCs from burning affected vegetation....inhalation of COCs within a lingering plume....."* Please discuss why these pathways were not considered further in the exposure assessment, as it appears only foliar contact was considered on page 36. Foliar contact was not a pathway listed in Figure 4-1.
  - 4th and 5th paragraphs: Reference is made to military personnel conducting *"maintenance activities such as felling dead trees, or clearing undergrowth."* It is further stated that *"for work crews and military personnel on manoeuvres in the area conservative default estimates of dislodgeable foliar residues and generic agricultural transfer coefficients will be used....."* This is the only place in the report that this receptor is discussed. This receptor and their possible exposure pathways are not included in Figure 4.1, nor are exposure estimates or hazard quotients calculated. It appears that this receptor is not a military scout or a military trainee. Please discuss why an exposure assessment and risk calculation was not completed for this receptor. See comments on the importance of considering this receptor above.
  - Remove words "staking, topping, training" from final paragraph on page 19. These words make no sense in this context as these activities are not relevant to the scenarios being assessed.
- Section 4.3.1.3, p20, On-site Military Trainee
  - Reference is made to inhalation exposure via impacted soil and dust yet this exposure pathway was not identified in Figure 4-1 nor considered in the exposure assessment for this receptor (Section 5.4.5). Consumption and dermal contact with water should be addressed (see above comments on water under civilian exposure for suggestions on how this could be done). Please clarify and explain which exposure pathways were considered and which were excluded. .
- Section 4.3.1.4, p20, Accidental Spray Event
  - Please discuss the uncertainty and conservatism of assessing this scenario. Comment on how the event is considered to be "unlikely." Please explain why there would be "no canopy cover protection" for this scenario. Provide a rationale for the extent of the conservative assumptions used and why.
  - It would help to discuss that for flaggers, any accidental scenarios that typically occur would have been captured in the PHED scenario.
- Section 4.3.1.5, p 20, Civilians

- See comments for Section 4.2 - Offsite Civilians. Please address water and drift as suggested in comments under Section 4.2.
- First paragraph - *text reads "Exposure events may occur .....as a result of spray drift migrating to off-site locations.*" Third paragraph - "*Civilian receptors may also be exposed to COCs as a result of herbicide spray drifting to areas outside of the military property line."* Please discuss the likelihood of this happening based on the results presented in the spray drift report (Task 2D) and considering the comments noted under Section 4.2.
- Third paragraph: "*Impacted groundwater may also be source of exposure as a result of the movement of volatile chemicals into indoor environments through vapour infiltration, or in cases where groundwater is used as a potable water source...."* As discussed in the comments for Section 4.2, please comment on the volatility of dioxins and HCB and the impact of this given the likelihood of groundwater being a source of exposure for the spray areas of 1966 and 1967.. Please refer to comments under Section 4.2.

Section 5.0 - Exposure Assessment

- "The primary objective of the exposure assessment is to predict, using a series of conservative assumptions, the rate of exposure....." This statement is too simplistic. Comment on why the primary objective is to be conservative. In general, conservative assumptions are applied in relation to the degree of uncertainty around that assumption. For each assumption the risk assessor needs to consider and document what information is available regarding that assumption and the extent of conservatism warranted based on the knowledge available. This allow the results of the risk assessment to be interpreted in proper context.
- Section 5.1 - Estimated Daily Intake (EDI)
  - See detailed comments for Appendix C below.
  - Please provide specific information on the historical and current background daily intake value for dioxins and HCB that would need to be included in the main report. For example, does the historical EDI represent the exposure in 1966 and 1967 or is it more representative of another time period? Describe the data that the current EDI is based on. For what years was the historical EDI used when determining body burden exposures? Similarly, for what years was the current EDI used? Also, it was unclear why a lifetime composite receptor was used instead of the adult, as only adult receptors are considered in the risk assessment.
- Section 5.2, first paragraph
  - As stated in the Statement of Work for this project, the U.S. EPA would also be a good source of information on exposure assessment methodologies.
- Section 5.3.1
  - It is unclear how it was decided which parameters would be estimated as single values and which would be represented by a range (high, low, central estimates). This is basically introducing probability into some variables and not into others. The report authors should indicate if all the variables were examined systematically to decide which should be treated stochastically (as a data distribution) and which to be treated deterministically (as a single point estimate), with consideration to which are driving the risk. A logical step in this process

would be some sort of sensitivity analysis, i.e., considering the effect on the results of varying the parameters over their expected ranges, to determine which parameters are most important.[1]

- Only "upper-case" is defined, while "central" and "low" are not. They warrant an explanation here. Is "central tendency" (in the subheading) the same as "central"?
- "The parameter that vary across each of the three exposure estimates are..." Neglects to mention 1) surface area of skin exposed, which was apparently treated as a range for the flagger accident and field scout scenarios, and 2) forest canopy interception factor, where a range was apparently used for the military trainee scenario. It appears the range was used only for one scenario, but the general statement in Section 8.1 implies otherwise by not being specific: "A range of canopy intercept factors were [was] employed."

• Section 5.3.1.1
  - "As previously discussed..." The reviewer could not locate where this was discussed. It would be helpful to give the report section number, as these are important assumptions in the exposure assessment.
  - Text states *"...a review of the scientific literature indicated that the PCDD content in Agent Orange was represented by a concentration of 2 ug/g."* It was not clear how the value of 2 was selected 2 from a literature review, or whether it was a Mean value, median, etc. Were all literature data given equal weight? What was the range or standard deviation? The only previous statement to be found was (p. 6): "All 2,4,5-T in Agent Orange was assumed to have a level of contamination by TCDD of 2 ppm." It was unclear what this assumption was based on, or why ? a range of PCDD content was used for Agent Purple and not for Agent Orange or picloram.
  - "The HCB content in picloram was determined to be 200 ug/g." No reference given for how it was determined, and not discussed earlier in Table 2-1 and 2-2. Please clarify the source of this value.

• Table 5-1:
  - Suggest adding "Estimated" to the title, as these values are not measured/known but represent your best estimate or assumption. Likewise for the titles to Tables 5-2, 5-3, and 5-4.
  - Values in table are expressed as a unitless fraction, yet elsewhere in ppm, then also in ug/g. Please use consistent units.

• Section 5.3.1.2 - Dermal Absorption
  - For dioxins, it is not clear which congener was the basis for deriving the dermal absorption value. For comparison with published, measured dermal absorption values (see below), it would be useful to also express estimated dermal absorption values as a rate or a percentage
  - When deciding which values to represent the upper, lower and central exposure estimates, comment on why these statistics were the only parameters considered? For example, would different congeners have varying absorption levels?

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[1] For an example of an analysis to determine the relative contribution of individual parameters to the overall risk estimates for dioxin exposure, see: Ma, H. "Using stochastic risk assessment in setting information priorities for managing dioxin impact from a municipal waste incinerator." Chemosphere 48 (2002) 1035-1040. This multimedia risk assessment had over 500 parameters, but through an uncertainty analysis, the authors identified the 15

- There are many published studies in which dermal absorption of dioxins was evaluated (e.g .those listed below). The results of these studies could be considered as part of a weight-of-evidence approach, by comparing measured and modelled values, to electing dermal absorption values for the low, central and high exposure estimates. Consider for example:
  - Anderson YB, Jackson JA, Birnbaum LS. Maturational changes in dermal absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in Fischer 344 rats. Toxicol Appl Pharmacol. 1993 Apr;119(2):214-20.
  - Brewster DW, Banks YB, Clark AM, Birnbaum LS. Comparative dermal absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin and three polychlorinated dibenzofurans. Toxicol Appl Pharmacol. 1989 Jan;97(1):156-66.
  - Banks YB, Birnbaum LS. Absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after low dose dermal exposure. Toxicol Appl Pharmacol. 1991 Feb;107(2):302-10.
  - Banks, Brewster, Birnbaum. 1990. Age-related changes in dermal absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,4,7,8-pentachlorodibenzofuran. Fundam. Appl. Toxicol. 15, 163-173.
  - Poiger H and Schlatter CH. 1980. Influence of solvents and adsorbents on dermal and intestinal absorption of TCDD. Food and Cosmetics Toxicology 18:477-481.
- A discussion of dermal absorption of soil-bound HCB and dioxins would be useful in the main report here, not just in the Appendix.

• Section 5.3.1.3
  - The personal protective equipment described in this section is not consistent with Page 18, 2nd paragraph (see above comments for section 4.3.1.1)
• Section 5.3.2 - paragraph 2
  - The incorrect conversion factor is cited for converting application rates from g/m^2 to lbs/acre. The conversion factor cited is 1.12E-01 whereas the correct conversion factor is 8.9. This suggests that the exposure estimates could be underestimated by factor of approximately 80 times. Unfortunately, sample calculations were not provided to verify whether this error actually occurred in the calculations. Please verify that the correct conversion factor was used in the calculations.
• Table 5-2:
  - The PCDD rates for Agent Orange appear to be under the “low” heading, when they are single-value estimates. Could move them to the left under “central”, or change the column headers.
• Tables 5-2, 5-3, 5-4 and 5-5:
  - The column of “application rate of a.i.” is misleading. The a.i. or active ingredients refers to the defoliant chemical, such as 2,4-D, that would be present in the product. Please specify whether this column represents the application rate of the active ingredient, of the entire product (e.g., Agent Purple) or of the contaminant.
  - Diesel is listed in Table 5-2 as a component of the applied mixtures but is not further addressed in the report. Is the intent to address this in the other tiers or to develop a rationale for its exclusion from the assessment?

- Section 5.4
  - Include the input values with each of the parameter definitions for the equations. For example, beside BW, please report which body weight value was used.
- Section 5.4.1.1
  - "*The PHED dermal UEs, which are an expression of the amount dermally absorbed by the receptor.....*" Replace "absorbed" with "deposited." PHED provides exposure estimates of dermal deposition, not dermal absorption.
- Tables 5-6, 5-7 and 5-8:
  - It is confusing to have "low, central, high" as the rows when the previous tables had these as the columns.
  - In addition to the column-row transposition, the order of the three estimates varies among the tables, which is confusing: Table 5-2 lists central, low, high. Table 5-6 lists low, central, high. Tables 5-9 and 5-10 list central, lower, upper (note different terms used).
- Section 5.4.1 and 5.4.1.2
  - Exposure Resulting from an Accidental Spill - This is the first time that this exposure pathway has been mentioned in the report. It was not included in 4-1. PHED scenarios for mixers/loaders include any routine spills and splashes. Please provide a rationale as to why an additional spill scenario was considered necessary for this assessment. This should include a rationale for the high degree conservatism used in the assessment (eg., spills would occur every day at the highest concentration).
  - The 30% clothing penetration rate applied here is not consistent with the 75% clothing protection factor used elsewhere in the report.
- Section 5.4.2
  - It would be useful to cite Technical Memorandum 141 (which identifies that one pilot applied all mixtures in about 30 hours of actual flying time over the three consecutive days, but does not identify the number of personnel involved in mixing and loading, or the number of flagmen.) Assumptions beyond what is actually known should be justified.
- Section 5.4.3, 3rd paragraph
  - Provide a reference for the following statement: "Generally, use of PHED UEs assumes that individuals involved in flagging activities are professionally trained."
- Section 5.4.3.2
  - Why was the factor of 2.7 chosen rather than the peak factors calculated by REMSpC's modelling? It is misleading to state that the factor of 2.7 is "based on an analysis provided by REMSpC" as it could be concluded that 2.7 was the peak factor from the modelling, when in fact 2.7 is from a 1964 report on calibration trials. The modelling predicted lower peak factors, i.e., Fig. 1 shows 1.4 for the 1966 trials and Fig. 2 shows around 0.85 for the 1967 trials.
  - Similarly, the definition of 2.7, following the equation, as "worst-case multiplier based on wind speed and direction" suggests site-specific data and modelling were used to generate this factor, which is not the case.
- Table 5-9:
  - Text cites canopy intercept factor of 0.9 with reference of Karch et al. 2004. It is unclear why 0.9 is listed in this table when 0 was used as described in the text.

- It would be useful to have "a Table 5-9", not just for the flagger scenario, but also for the mixer/loader and applicator scenarios.

• Section 5.4.3.3
  - Please comment on why an alternate exposure assessment methodology was utilized for the flagging activities, including the reference for the alternate approach (if any), what are the strengths and weaknesses of both approaches (PHED vs alternate approach), inherent conservatism and uncertainties, and validation and acceptance of both methods.
  - 2nd paragraph - PMRA is misquoted. "PMRA (2006) indicated that within an agricultural setting approximately 20% of the aerial application rate would reach the soil surface." This statement would be correct as follows: "PMRA (2006) indicated that within an agricultural setting approximately 20% of the application rate is dislodgeable from foliage immediately after application." Since dislodgeable residues from foliage is not the subject of this paragraph, the entire sentence is irrelevant and should be deleted.
  - For aerial applications to forestry, the PMRA uses a 50% interception factor to calculate buffer zones. The drift modelling in the spray drift report did not assume any interception. As noted by Cantox, the published literature indicates most of the application would likely be retained in the upper canopy under dense foliage conditions.
• Section 5.4.4
  - As noted in the Statement of Work for this contract, PMRA has produced a guidance document on the principles/theories of estimating potential exposure using dislodgeable foliar residue (DFR) data and agricultural transfer coefficients (TCs) for estimating potential exposure to people entering areas treated with pesticides, including areas similar to forestry scenarios (Post-application Exposure Monitoring Test Guidelines (PRO98-04) available at http://www.pmra-arla.gc.ca/english/pubs/pro-e.html). Additional information on this topic is generated by Exposure Task Forces and can be found at: www.exposuretf.com and on the websites for PMRA and the U.S. EPA. Cantox estimated exposure to the field scout using a method developed by the USDA Forest Service. It would be useful to include a discussion in this section of the USDA exposure assessment methodology versus the standard methodology used by the PMRA and the U.S. EPA, including what are the strengths and weaknesses of both approaches, inherent conservatism and uncertainties, and validation and acceptance of both methods. Also discuss how the transfer rates are derived for both methods and whether it is validated based on actual data.
  - Text reads *".....a fraction of dislodgeable residue of 0.1 was used....."* Please specify fraction in relation to what (the application rate?) and indicate how this value was derived.
  - *"The time period assumed between initial spray operations and re-entry into each plot was short enough to ....."* Please specify what the time period was. Also specify the chemical-specific transfer rate that was calculated. Please discuss how/why it is chemical-specific.
• Section 5.4.5, Military Trainees
  - *"Military trainees were assumed to spend 2 months of the year at the 1966 spray campaign site."* It is unclear what this assumption is based upon, and whether

this is an average estimate, or is it longer than average, i.e. conservative.

- 1st paragraph: the exposure pathways listed are not consistent with Figure 4-1.
- Please provide a rationale as to why exposure pathways from surface water and groundwater were not considered. See comments about regarding exposure from surface water and groundwater for civilians.
- Was exposure from dermal contact with foliage considered?
- 2nd paragraph: What soil half-lives were used? Were the phys/chem data generated in Task 2A used?
- 2nd paragraph: Degradation of PCDD was not discussed previously in the report.
- Page 38, 1st equation: the units do not cancel. The units of soil bulk density are kg/m^3 and it appears that a conversion factor needs to be included.
- Page 38, 2nd equation: terms defined include $t_{1/2}$ but $t_{1/2}$ is not used in the equation, the rate constant k is used instead. To define k in terms of $t_{1/2}$, please create a separate equation. For cross referencing, it would help to number all the equations in the report.
- Page 38, 3rd equation: units do not cancel. Clarify the units for wild berry consumption (currently cited as g/kg/day). Also the study bioavailability would not be unitless in order for the units to cancel in this equation.
- Page 39, 1st equation: include a conversion factor to allow units to cancel.
- Page 39, 2nd equation: units do not cancel. In order for the units to cancel, the units for soil adherence factor should be $g/(cm^2\ day)$ and the dermal absorption factor would not be unitless.
- The exposure equations on pages 38 and 39 include division by an averaging time of 1095 days. Justification should be provided as to the appropriateness of the use of this averaging time when calculating the HQ for the acute exposures.
- Table 5-11: Please clarify whether consumption of berries is assumed to occur every day for 60 days per year, and the basis of that assumption.

• Sections 5.5.1 - 5.5.3

- Text reads *"As described in Section 5.3.1, the low, central and high exposure estimates were..."* . Report lists exposure parameters considered as a range but does not include canopy interception factor, which was also treated as a range for some scenarios (military trainee). A clearer summary of all the variables considered as a range for each scenario (a table perhaps) would be very helpful. Sections 5.5.4 (scout) and 5.5.5 (trainee) do not make any mention of which variables were considered as a range to arrive at three estimates.
- Based on the manner in which the equations and data are presented in the report, the calculations cannot be verified. Many of the equations in the report are difficult to understand as the units do not cancel. Inputs for the equations are not readily available; the reader has to search through the report and find some of these inputs in the appendices.
- It is recommended that sample calculations be provided such that at least one calculation per table for the exposure and hazard quotient calculations can be followed through. In addition, the footnotes of the tables should include the equations used and inputs for the equations, including the toxicity reference value.
- The spread between "low" to "high" estimates is up to five orders of magnitude. Please comment on this and how it impacts characterisation of

the exposure and risk estimates.

Section 6 - Hazard Assessment

- Section 6.1 Hexachlorobenzene
  - p. 45 - the first paragraph could note the fact that HCB was assessed by Health Canada to be a probable human carcinogen and declared toxic under CEPA in 1993 and that it was subsequently added to the Prohibition of Toxic Substances Regulations under CEPA in 2003, rather than using the Barber 2003 reference that has been cited here.
  - p. 46, 1st paragraph - *"Animal studies have...risk for cancer of the liver, thyroid and kidney."*
  - p. 47, 1st paragraph - *"CEPA (1993) reports a TD_{05}..."*, cites the wrong 1993 reference in the list of references at the back of the report. This information is taken from the 1993 CEPA assessment for HCB (ISBN 0-662-20291-0) not the 1993 Health Risk Determination publication cited.
- Section 6.2 Dioxins
  - p. 48: "Selected Exposure Limits" would be more accurate as "Toxicity Reference Values."
  - p. 49, 4th paragraph - "Previously...assuming first-order elimination ranging from 7- 9 years in adults.", i.e., more recent information indicates that elimination rates in infants may be as little as months, so there is variation in these rates depending upon age/other factors.
  - p. 52, last line - "Several other countries have or had recommended the same TDI, including the WHO (1991), the UK...", i.e., the value referred to here, of 10 pg/kg bw/day, is no longer recommended by the WHO or many other health agencies, most including the WHO, having replaced this value with a considerably lower one.
  - p. 53, 1st bullet - "...Between 5 -11 years in adult humans.", i.e., same comment as above.
  - Table 6-1 Heading - should be "Tolerable" vs. "Acceptable"
  - p. 54, 3rd paragraph - "(Canadian Environmental Protection Agency, 1997) ?? isn't listed in the list of references. Was it meant to refer to the 1990 CEPA dioxin assessment?
  - p. 54 , 4th paragraph - it would be useful to have in the main report, a description of the study from which the short term MRL of 200 pg/kg/day was derived by ATSDR.
- p. 59, Section 6.3.1, Specific Health Effects Associated with Agent Orange/Purple
  - this section mentions only carcinogenic effects, and none of the other effects such as diabetes, cardiovascular disease, chloracne, spina bifida, etc. Should either modify the title or add the other effects.
  - p. 59 - 62: the conclusions of the IOM are highlighted in italics throughout, but the text in the preceding paragraphs generally would support a different conclusion, rendering the italicized text non-sequiturs. There needs to be some background included as to the rationale for the IOM's seemingly contrary conclusions.
  - p. 62 - Other Cancers: should add female reproductive cancer (cervix, uterus,

ovary) to this list.

- p. 63, Section 6.3.1, Evidence of Health Effects Associated With Agent Orange/ Purple Exposure
  - there is considerable repetition of much of what is in section 6.3.1, i.e., these sections could be better organized and the headings should be re-worked.
- Section 6.2.5 - Body Burden of Dioxin and 7.2.5 Dioxin Body Burden Calculations
  - The whole weight blood values described in section 6.2.5 from the CDC survey should be in fg/g units and not pg/g.
  - p. 57, Table 6-5 - The current background human tissue level of dioxin TEQs (Table 6-5) may be overestimated at 22.8 pg/g lipid. Ryan et al. (Food Add. Cont., 10(4):419-428, 1993) reported an average TEQ value based on a pool of 200 Canadian human milk samples collected in 1981-82 as 24.7 pg/g. This value had decreased to 15.6 pg/g lipid for human milk samples collected in 1986-87.
  - As such, the estimated dioxin TEQ tissue concentration of 21.8 pg/g from the average daily intake figure of 1.8 pg/kg bw/day may be underestimated. Peak dioxin environmental loadings probably occurred from 1960-70 so highest human tissue concentrations would be expected in the early 1970's. This is supported by data from Lunden and Noren (Arch. Environ. Cont. Tox., 34:414, 1998). Average TCDD levels alone from U.S. adipose samples collected in the early 1970's were approximately 18 pg/g (Aylward and Hays, J. Exp. Analy. Environ. Epi., 12:319, 2002). An earlier TEQ estimation, previously provided to DND was approximately 50 pg/g lipid, based on Canadian human milk data, and is comparable to the range recommended by Lorber (Sci. Tot. Environ., 288:81, 2002) for the U.S. population during the 1970's (50-80 pg/g lipid). A background dioxin serum concentration of 50 pg/g lipid would result in an approximate total body burden of 12.5 ng TEQ/kg bw. Using the estimated absorbed dose from Table 7.1 of 30 ng/kg bw/day (single day exposure), a BB of 12.5 ng/kg bw would increase to a BB of approximately 42.5 ng/kg bw or a TEQ lipid value of 240 pg/g lipid.
  - A general recommendation would be to express all body burdens on a per kg bw basis to avoid confusion between actual body burden and tissue concentrations reported on a pg/g lipid.
  - A good comparison, from a risk perspective, is to the Ranch Hand cohort. A recommendation would be to list the various health affects in combination with the estimated body burdens.

Section 7 - Risk Characterization

- 1st paragraph - regarding the statement “plausible range of exposures”. Please refer to the general comments above on the importance of interpreting results in the context of conservatism and uncertainty. Please comment on the plausibility of spreads of four to five orders of magnitude in estimates for the same scenarios and what such uncertainty means for the risk assessment.
- Table 7.1. It could be useful to compare the body burden estimates with the measured values for Vietnam Veterans presented in Tables 6.6/6.8. It might be possible to assess how the estimated body burdens compare with those measured for Vietnam Veterans who

did and did not participate in the Vietnam spray program. It might also be useful to recommend measuring dioxins/lipid for some of the individuals who had possible higher exposures to validate the range of estimated values (see additional comments under conclusions).

- Section 7.1 - equation - please clarify what the absorption factor is, i.e, absorption into what tissue?
- Section 7.2.1
  - "Several risk estimates exceed levels that would be indicative of a concern." Please state which ones – otherwise you make the reader do the work of looking in the tables to identify values >1.
  - Last sentence: "HQ estimate for... the flagger scenarios were quite elevated..." Actually, the PHED flagger scenario is < 1 except for the "high" estimate, while only the alternate flagger scenario exceeds 1 significantly. It is unclear why there is such a large difference between PHED and alternate method and which would be more valid. These results need interpretation and discussion.
  - Similarly, the elevated HQs for the mixer/loader "accident" scenarios need more context with respect to their conservatism, as the estimates derived from PHED already incorporate the spills that happen during open mixing/loading.
- Tables 7-2 through 7-8 and 7-11 through 7-24:
  - It would help to bold or underline the values that exceed risk benchmarks.
  - It would also be useful to present HQs and body burdens relative to background exposure and relative to the body burdens that have been associated with observed adverse effects in humans. . This would help answer the question of what is the contribution of risk from the Gagetown scenarios compared to background risk for the Canadian population.
- Section 7.2.3:
  - The wording relating body burden versus possible risk is clearer her and should be replicated elsewhere (per comments above). However, please provide more details on the recommendation for an epidemiology study. Please clarify what "who were present in the vicinity" means. Is the exposed group big enough to design an epi study with any power? Would it be more useful to investigate the utility of the existing ranch Hand studies to the Gagetown scenario?
- Section 7.3.1
  - Please specify whether background exposures for HCB were added into the exposure estimates and that is the basis for comparing the HQ to 1

Section 8 - Uncertainties

- Section 8.1
  - "...the central tendency represents the most likely case." How does this methodology compare to risk assessments that have exposure estimates representing the 95th % Upper Confidence Limit of the mean?
  - This section lists the assumptions that have uncertainty, but provides no context for interpreting the effects of such uncertainty on the resulting risk estimates. Suggest adding discussion including sensitivity analysis of the effect of these assumptions on the results. This bulleted list leaves little assurance that the

assumptions collectively lead to a conservative (protective) estimate of risk.

- How would the incremental risk added by considering a worst-case scenario for surface water and/or groundwater affect the existing range between the low-central-high risk estimates? It might help to discuss the risks from the various exposure pathways to put them into perspective, especially with regard to the overall uncertainty in the assessment (as reflected by the range).
- Suggest discussing the possibility of cumulative risk posed by exposure to both dioxins and HCB.

• Section 8.2
  - Bullet 5 - The uncertainty factor for the long-term dioxin TDI is 10. Ten is debatable in terms of whether it is a large uncertainty factor.

Section 9.0 - Conclusions and Discussion

• Conclusions section is confusing. A re-structure with sub-headings such as acute and chronic wold help. For example, the second bullet could be a sub-point under the first bullet as both deal with acute exposure. It is unclear if the conclusions are based on the central exposure estimates. Sometimes the "high end" estimate is invoked, when it indicates risk. It may be better to organize the conclusions by receptor group rather than by chemical.
• Structuring results by chemical emphasizes that the risks were evaluated separately. It is unclear what the cumulative risk from exposure to both dioxins and HCB (if this was possible) would be? Would this be calculated by summing the HQs?
• Dioxins
  - 1st bullet - "Acute effects examined through this evaluation have been classified as 'less serious' by ATSDR." - the way this is written, it suggest that the effects have no connection with the exposure levels. For clarity, it would be better to say, "The acute effects associated with these levels are among those classified as 'less serious' by the ATSDR."
  - The second bullet seems to be definitive ("some individuals may have experienced effects"), even taking into consideration the uncertainties described. The fifth bullet could include possible biological monitoring of individuals who were estimated to have been involved with mixer/loader accident scenarios.
  - 3rd bullet - "...as a result, no dioxin related adverse health risks <u>are predicted</u> for military trainees...". Again, this is the wrong tense, in view of the fact that we are looking at past risks. It would be better to use a time-independent verb, such as "would be expected".
  - 5th bullet - it is recommended that further epidemiological investigations focussing on individuals who were present in the vicinity of the 1966 and 1967 spray applications, be undertaken. An alternative approach might be to recommend serum dioxin analyses for these individuals where possible, particularly for the two occupational categories highlighted. These data could then be compared to the body burdens of Vietnam veterans, etc. and to the associated epidemiology and health studies.
• Hexachlorobenzene
  - Last bullet "ILCR estimates for the central tendency receptor are essentially

equivalent to the benchmark for the 1967 spray period." Meaning is unclear. Should be reworded to clearly indicate what is meant by the "benchmark" the ILCR estimates are being compared to.

- The section is called "Conclusions and Discussion" yet there is very little discussion.

References:

- CDC. 1998 - appears to be the same as ATSDR. 1998. - please verify
- Demaree and Creager - should be 1968, not 1968a
- Demaree and Haws – should be 1968, not 1968b
- Health Canada. 2004. Federal Contaminated Site Risk Assessment in Canada. Part I: Guidance on Human Health Preliminary Risk Quantitative Assessment Health Canada..... - should become Health Canada. 2004a. This reference has been cited on numerous occasions in the text while citing TRVs. The proper reference in those cases should be: Health Canada. 2004b. Federal Contaminated Site Risk Assessment in Canada. Part II. Toxicological Reference Values (TRVs). Environmental Health Services. Safe Environments Program. September 2004.
- Health Canada. 2005. Please insert "Factsheet" in the citation.
- IARC. 1997. Citation incomplete - please insert : Volume 69. Polychlorinated Dibenzo-para-Dioxins and Polychlorinated Dibenzofurans. Summary of Data Reported and Evaluation.
- Karch et al. Typo "Cietnam"
- PMRA, 2005. This reference is not cited anywhere in the report.
- PMRA. 2006. Personal Communication with Mary Mitchell – suggest providing her title and division.

Appendix A:

Major comments:

The following Canadian reviews on pentachlorophenol and its contaminants should have been consulted during the preparation of these comments, to obtain additional data sources for levels of impurities in PCP formulations:

- Jones, P.A. (1981). Chlorophenols and their Impurities in the Canadian Environment. Report EPS 3-EC-81-2, Environment Canada, 434 pp.
- National Research Council Canada.. 1982. Chlorinated phenols: Criteria for environmental quality. NRCC No. 18578. 191 pp.
- Gilman, A.P.; Douglas, V.M.; Newhook, R.C.; Arbuckle, T.E. (1988) Chlorophenols andtheir impurities: a health hazard evaluation. Health and Welfare Canada.. Document No. H46-2/88110E.

Based on the above reviews, additional dioxin levels in American PCP products, should be provided and considered for the exposure and risk assessments. For example, papers from Rappe et al (1982), Nilsson et al, (1978), Rappe et al (1978), Rappe et al (1979) and Arsenault et al (1976) all contain such information.

Specific comments (typos and minor insertions are generally noted in bold fonts):

- The main report text needs to reference this appendix where appropriate
- Section A1-1.0 Pentachlorophenol
  - Page A-1, para.. 1, last sentence states: "The use and uncontrolled incineration of technical grade PCP is one of the most important source (typo, singular) of PCDDs and PCDFs in the environment". Please provide reference for this statement. This statement may have been true at one time in the past but the current uses of PCP are strictly limited to industrial uses (heavy duty wood treatment). Reference: Agriculture Canada.. 1992. Re-evaluation of heavy duty wood preservatives. Announcement A92-02. Available at: http://www.pmra-arla.gc.ca/english/pdf/rev/rev_a9202-e.pdf)
  - Page A-1, para. 5 states that: "The water soluble form of PCP (pentachlorophenate **salt**) generally had lower concentrations of PCDDs and PCDFs when compared to organic soluble **penta**chlorophenol. However, Table A1-1.1 clearly shows that detectable amounts of TCDDs (0.05-0.25ppm) were ONLY found in Na-PCP samples. This is also contrary to the statement below table A1-1.1 : "These reports all agree that the lower substituted congeners (....) were below the detection limit. These unexpected results were later found to be an unusual 1,2,3,4- substituted isomer (Buser and Rappe 1978 in: Rappe et al 1982). Please revise the text accordingly.
  - Page A-2, Table A1-1.1. In the title, please replace the term "commercial" by "commercially available". Commercial grade PCP was a formulation that contained up to 20% tetrachlorophenol, a product very different from the technical grade PCP that was available at the time (REF).
  - Page A-3, Table A1 1.2, title, as above
  - Page A-3, Table A1 1.3. Title: please change to .... based on Tables A1-1.1 and A1 1.2
  - Page A-3, Table A1 1.3. The values in the min and max rows are inverted
  - Page A-3, Table A1 1.3. last row: "Total ppm by TEF" should read : Total ppm **as WHO-TEF**
- Section A1-2.0 2,4,5-Trichlorophenoxyacetic Acide (2,4-T)
  - Page A-4 states "one sample of 2,4,5-T contained about 27 ppm..." but Table A1-1.4 reportedly citing the same study (Elvidge, 1971) does not list any TCDD concentration greater than 0.50 ppm. Additional information is provided by Firestone et al (1978) who reported levels of 2,3,7,8-TCDD in stored drums of Agent Orange (before 1970), and estimated levels as high as 100 µg/g (100 ppm) in individual 2,4,5-T formulations.
  - Page A-6: para. 4: Edmunds et al (1973) in not cited in the reference section.
  - Section A1-2.1 Agent Purple, Page A-6: It seems very probable that the dioxin level (45 ppm) reported by Young et al. (2004) in a single agent purple sample would be referring to the same sample reported earlier as 45 ppm TCDD by the same author. Please verify. The "Detrick" reference is not cited in the reference section
  - Page A-6: Agent Orange weighted mean concentration of TCDD was 1.98 ppm. But the maximum detected was 15 ppm, so using 2 ppm is not a worst case, i.e., the TCDD content could have been higher. Why was a range used for Agent

Purple and not for Agent Orange, when there are data on the range measured in Agent Orange?

- Page A-7 states "For the purposes of the current assessment all 2,4,5-T in Agent Purple should be assumed to be contaminated at a level of 45 ppm TCDD." In the report, however, a range of 5 to 45 with a central estimate of 32.8 ppm is used.
- Report text needs to reference this appendix where appropriate.

Reviewers' citations for Appendix A:

Arsenault, R.D. 1976. Pentachlorophenol and contained chlorinated dibenzodioxins and dibenzofurans in the environment. A study of environmental fate, stability, and significance when used in wood presenvation. Proceedings of the American Wood Preservers Association 20: 122-148. (Reporting levels in American products)

Firestone, D. 1978. The 2,4,7,8,-tetra..... problem: a review. Ecol. Bull. (Stockholm) 27: 39-52

Rappe, R.D., Gara, A. And Buser, H.R. 1978. Identification of polychlorinated dibenzofurans (PCDFs) in commercial chlorophenol formulations. Chemosphere: 12: 981-991

Rappe, C., Buser, H.R. and Bosshardt. 1979. Dioxins, dibenzofurans and other polyhalogenated aromatics: production, use, formation and destruction. N.Y. Acad. Sci 320: 1-18

Rappe, C., Nygren, M., Buser, H.-R., and Fauppinen, T. 1982. Occupational exposure to polychlorinated dioxins and dibenzofurans. In: Chlorinated Dioxins and Related Compounds: Impact on the environment. Hutzinger, O., Frei, R.W., Merian, E. and Pocchiari, O. (Eds.). Pergamon Series on Environmental Science, Vol. 5., Pergamon Press, Oxford, England. Pp. 495-514.

Appendix B

- Major comment: Dioxins and furans are not the only contaminants found in PCP formulations. HCB is also generated during the manufacture of pentachlorophenol (for example: Canada Gazette (1991), volume 135, No 39; Rappe et al 1982). Please provide information on the HCB content of PCP formulations. This information should be taken into account in the exposure and risk assessments.

- Table B1-2, Chem/Phys properties of TCDD:
  - Many of these values are different from those in Task 2A, Table A-1, which were supposed to provide a common database for all other tasks. The two sets of phys/chem values should be reconciled.
  - TCDD half-life in soil is listed as 10,000-30,000 hours, which converts to a range of 1.1 to 3.4 years. What is the value in parentheses - an approximate mean? The half-lives in soil vary over a wide range; was this range reflected in the exposure assessment calculations of soil concentration 1 year after spray event (p. 38), or was a single value used? It is unclear where the values were used. Using the low end (10,000 hours), the fraction remaining after 1 year is 0.54, while using the high end (30,000 hrs), the fraction remaining after 1 year is 0.82. How

sensitive is the risk estimate to this range?
- Half-life in sediment water is listed as >30,000 hours. This converts to 3.4 years, which does not match value in parentheses (~6 years).
- Text on page B-37 states that half-lives in soil and sediment range “from 2 to greater than 6 years”. Not consistent with Table B1-2, which has 1.1-3.4 yrs for soil, and >3.4 years for sediment.

- Table B2-2.1: Chem/phys properties HCB
  - Values are different from those in Task 2A, Table A-1.
  - Half-lives in soil in table are referenced as Mackay et al. 1992, but half-lives in soil on page B-76 are referenced as Griffin and Chou, 1981.

- Page B-7, para. 2: the reference "COT 2001" should be presented as "UK COT 2001" to conform with the citation in the reference section. Please review the entire Appendix B and make the appropriate changes
- Page B-8, last para., last sentence ".... are summarised in Table B1-3.1. Do you mean Table B1-3.3 ?.
- Page B-9, first sentence: "Table B1-3.3....". Do you mean Table B1-3.4 ?.
- Table B1-3.4: make the following insertion in the title: "Summary of Human Health effects of 2,3,7,8-TCDD Exposure"
- Table B1-3.4: Summary of effects of 2,3,7,8-TCDD Exposure, comments for Respiratory effects: please provide specific references for "....other occupational studies" (line 5); "Operation Ranch Hand and follow-up cohort studies of those involved in Seveso...." (line 6)
- Table B1-3.4: Summary of effects of 2,3,7,8-TCDD Exposure, comments for Renal effects: please provide specific references for :" Similar to other studies..." (line 4)
- Table B1-3.4: Summary of effects of 2,3,7,8-TCDD Exposure, comments for Dermal effects: please provide specific references for :"Studies of a chemical laboratory (line 4 and others in the same sentence.
- Table B1-3.5: Please provide units for the exposure duration (1st column)
- Page B-12. 1st para., line 4: the "COC, 2001" should be presented as "UK COC 2001" to conform with the citation in the reference section. Please review the entire Appendix B and make the appropriate changes.
- Page B-15, para. 3, line 13.: Please define "ED01"
- Page B-17, para. 2. "In an NTP study completed in 2003 (NTP, 2004a, b, c, d)...". Four references are listed. Which is the correct one?
- Page B-17, para. 3. Again 4 references are listed. Which is the correct one?
- Page B-20 . Table B1-3.6: Significant Exposure to 2,3,7,8-TCDD. Which animal species were studied? Also please provide references in every case.

- Section B1-4.1 Absorption
  - Most of the references in this section are quite old. Please provide more updated information and revise text.
  - Page B-21, 1st para. It is surprising to find an MOE (1985) reference to provide such information. Please use more appropriate recent references.
  - Page B-22, para. 2 and 3: Please provide references for those 2 paragraphs as it is unclear if all the information presented here is from Dann (1989)

- Page B-24 - See comments for main report regarding body burden.
- Page B-25, last para.: What does AUC stand for?
- Page B-27. Insert a blank line to separate first 2 paragraphs
- Page B-30, 2nd para. Health Canada is in the process of re-evaluating the TRV for "dioxins" but provisionally the Food Directorate uses the FAO/WHO JECFA TMI of 70 pg TEQ_{DFP}-WHO_{98}/kg bw/month (TEQ includes dioxins, furans and dioxin-like PCBs) which corresponds to 2.3 pg TEQ_{DFP}-WHO_{98}/kg bw/day.
- Page B-38, last para., line 3: please replace "principle" by "principal"
- Page B-76:
  - "The average half-life of HCB estimated from results of a number of studies is ~9 years." What type of half-life? Soil (aerobic or, anaerobic), or water?
  - HCB half-lives in soil vary over a range; was this range reflected in the exposure assessment calculations of soil concentration 1 year after spray event (p. 38)? The values could not be located

Appendix C

Major comments:

- An average daily intake estimate of PCDD/DFs and dioxin-like PCBs via food consumption specifically for adults has not been calculated to estimate current exposure levels. Instead, the present day average exposure estimates of PCDD/DFs and dioxin-like PCBs through food consumption are given in the form of just one value, "0.88 pg TEQ/kd/day" for all Canadians (all age groups and genders combined) from the Total Diet Study (1992 to 1999). This mean value, calculated by the Food Safety Division, comprised all the individual daily food intake rates from all the respondents from the Nutrition Canada Survey (1970-1972) that were combined the respective contaminant levels in each of the analysed food composites (Personal communication from Dr. Xu-Liang Cao, Food Research Division, Bureau of Chemical Safety, Health Products and Food Branch, Health Canada). The resulting EDI, "0.88 pg TEQ/kd/day", is the overall mean calculation for all individuals, regardless of age or gender. It is not a calculated lifetime EDI weighted by age as inappropriately presented in Tables C1-1.6 and C1-1.7. It was unclear why a lifetime composite receptor was used instead of the adult, as only adult receptors are considered in this risk assessment. In addition, more background information on the Total Diet Study and the Nutrition Canada Survey should be provided in this Appendix (see Cao, 2005).
  - Therefore, adult age-specific DLC (dioxin-like compounds?) intake estimates should be calculated using a complete set of data on levels of DLCs detected in analysed food commodities from the Total Diet Study (1994-1995 and 1995 to1999). These latter, more recent concentrations of DLCs were provided to Mr. Elliot Sigal of Cantox Environmental Inc. on January 5, 2006 by Ms. Deborah Schoen of Health Canada regarding Cantox (2006). These data were obtained in a personal communication from Dr. Jake Ryan (Senior Research Scientist, Food Research Division, Bureau of Chemical Safety, Health Products and Food Branch, Health Canada). Please contact Health Canada to obtain these data sets if they are currently unavailable.
  - For the background values for the other exposure media (air, water and soil)

please provide additional information on the data sets: dates, types of surveys, complete references, etc.... In addition, provide a discussion on how representative the historical EDI represent the exposure in 1966 and 1967 or if it is more representative of another time period?

- A review of previous Canadian exposure assessments to dioxins and furans has not been performed. What is the rationale for this data gap? A good starting point would the exposure assessments presented in the 1990 CEPA report. Other papers by Birmingham et al (1989a; b) and Ryan et al (1997) should also be considered.
- Throughout this appendix, it is difficult to compare various estimated daily intakes as they are either reported as a daily intake (x pg/day) or on a body weight basis (x pg/kg bw/day), sometimes in the same sentence. Please report the intake data in a consistent manner.
- Please note that all the above major concerns/comments also apply to HCB.
- The notable downward temporal trend in the DLC concentrations in various environmental media, even during the last decade, should be presented and discussed, when possible. For example, consider presenting Figure 23 from Cao et al (2005) to show the trend over 8 years. For example, Lorber(2002) and Aylward and Hays (2002) provide empirical evidence of this downward trend.

• Minor comments and typos (typos and minor insertions are generally noted in underlined bold fonts):

- Appendix C cover page title “Estimated Daily Intakes” is too vague. Consider replacing it by something like: “Current Estimates of Daily Intakes of Dioxins and HCB for the Canadian General Population”
- Section C1-1.0 Canadian Population Dioxin Estimated Daily Intake
- Page C-1, first paragraph states: “Estimated daily intake rates of PCDD/PCDFs for the Canadian general population were calculated in 2006 by Cantox Environmental Inc.”. Please provide more information on the context of that contract report and the reference.
- Page C-1, Table C1-1.1, the reference Health Canada (2004a) and all those cited as “Source” are not cited in the reference section.
- Page C-1, last paragraph, first sentence should read “Average food intake rates.....”
- Page C-1, last paragraph, 2nd sentence should list the name of the cities as well as the dates of sampling
- Page C-2, Table C1-1.2 title: the reference Health Canada (2006) is not cited in the reference section.
- Page C-4, para. 1, last line; The reference should be cited as Cao et al (2005), not as Xu-Ling et al. 2005). Please make the corresponding changes in the text and in the C1-2.0 reference section.
- Page C-4, Table C1-1.4 title: please insert: “.....PCDD/PCDFs and dioxin-like PCBs for....1999". Furthermore, as indicated in the general comments of this appendix, this table must be completely reworked to present current “adult” EDIs
- Page C-4, para. 3, lines 1 and 2 : the soil background level should be expressed as 4 pg WHO-TEQ/g soil (dry wt).
- Page C-4, para. 3, states that: “This value (of 4 pg WHO-TEQ/g soil (dry wt) from the previous sentence) is based on the highest mean background

concentration for Canadian soils of 5.0 pg TEQ/g". This statement is unclear: please re-phrase and/or provide more information.

- Page C-4, para. 3, reports a U.S, EPA value of 3.5 pg TEQ/g for rural background (U.S. EPA 2000). However, in Table C1-1.8, US EPA (2003) reports a current background (rural or urban?) level of 9.3 pg TEQ DF-WHO98/g in soil. In addition, a background concentration of dioxin-like PCBs is reported to be 2.3 ppt TEQ p-WHO98. U.S. EPA (2003) is the revised draft version of the U.S. EPA (2000) draft. Which value is the correct one? Would the units be different?
- Page C-5, Table C1-1.6: please provide an example of full calculations to arrive at "Historical" estimated EDIs, otherwise it is impossible to verify any of the calculations.

• North American Population Dioxin Estimated Daily Intake
  - Page C-7, Table C1-1.9: please provide average body weights for each age group.
  - Page C-7, Table C1-1.9: first row, last column - typo: WHO

• Historical Dioxin Levels
  - Page C-8, Table C1-1.10: please expand this table to provide the historical concentrations used to calculate the historical EDIs (similar to what was done in Table C1-1.8)
  - Page C-8, the last paragraph actually presents the results of a pharmacokinetic modelling exercise performed by Pinsky and Lorber (1998). The last sentence states: " This dose (1.5 to 2.0 kg/kg/day) may have dropped to as low as 0.1 pg/kg/day (7 pg/day) and less into the 1980s". How do you reconcile these estimated results with those presented in Table C1-1.10? The more recent modelling results from Lorber (2002) and Aylward and Hays (2002) would have been much more appropriate.

• Section C2-1.0 Hexachlorobenzene (HCB) Estimated Daily Intake
  - The major comments (lifetime receptor, ...) outlined above for PCDD/DFs also apply to hexachlorobenzene. Please revise text accordingly. This entire section is essentially based on the Priority substances list assessment report for HCB published in 1993. Cao et al (2005) is the only new reference added to this section. Please perform a literature review to identify new data sources to present a more current exposure assessment.
• Health Canada Total diet Study
  - Table C2-1.1 reference should be Cao et al. (2005)
  - Table C2-1.2: it is incorrect to calculate weighted averages for HCB because the exposure varies according to diet age-specific diet. Please calculate arithmetic means for each age class based on the results presented in Table 10 from Cao et al (2005)

• Canadian Environment Protection Act
  - Page C-11: the above section heading is misleading. Please consider "Priority substances list assessment report for HCB"
  - Page C-11: please indicate that all the results from this section were taken verbatim from the assessment report

- Table C2-1.3: the reference “Environment Canada, 1993" for this table and there after should read “Government of Canada/Health and Welfare Canada/Environment Canada (1993)” or CEPA (1993)

- Historical and Current HBC EDI - Table C2-1.5 is identical to Table C2-1.3: why was it necessary to present it again?
- Section C1-2.0 References - Dann, Tom : please provide his title, affiliation, etc.

Citations for Appendix C:

Lorber, M. 2002. A pharmacokinetic model for estimating exposure of Americans to dioxin-like compounds in the past, present and future. Sic. Total Environ. 288: 81-95

Aylward, L.L. and Hays, S.M. 2002. Temporal trends in human TCDD body burden: Decreases over three decades and implications for exposure levels. J. Exp. Anal. Environ. Epidemiol. 12: 319-328.

Birminghan et al. 1989a. Chemosphere 19: 507-512

Birminghan et al. 1989a. Chemosphere 19:637-642

Ryan et al. 1997. Organohalogen Compounds 32: 229-232

Comments on Style and Grammar:

Some suggestions to include the readability of the report are

- Minimise the use of phrases such as “It is important to recognize...”, “It is important to note...”, “It should be noted that...”, “It is important to understand that...”, “It should be borne in mind that...” These phrases make the document seem ponderous and pedantic.
- Minimize overuse of subjunctives such as “should” and “would.”. On seeing “should” in the report, readers may ask “Why?” For example, if the report states that a certain assumption “should be” or “must be” made, that could mean many things – because of a lack of data, because Cantox is choosing a protective or conservative value, because of a regulatory requirement, etc. Suggest replacing should/must with the more precise reason for the action or decision taken whenever possible. As for “would”, usually it can be replaced by a more definite statement. Some specific examples:
  - Section 7.2.1: “Several risk estimates exceed levels that would be indicative of a concern (HQ > 1).” Why not use “are” instead of “would be”?
  - P. 3: “...data... should be comparable” Who judges the data to be comparable? Cantox?
  - P. 6, Table 2-2 footnote: “This should reflect the concentration...” Do you mean “This was assumed to reflect the concentration...”?
  - P. 17 “...half lives of the COCs would need to be considered...” Why not simply ‘were considered’?
  - P. 18: “...conservative assumptions must be made...” Why?
  - P. 88: “... assumptions should be made...” Why not simply state “assumptions were made”?

- "Since" is sometimes used when the proper term is "because." "Since" indicates time elapsed. "Because" indicates a reason or explanation. Example: Since the report was issued, we have discovered some errors. Because the errors were discovered, we will revise the report.

Typographical Errors:

- Word consistency: Both TIER and Tier are used in the report. Tier is correct because the word is not an acronym so there is no reason for it to be all capital letters.
- ES-2.0 "defense" should be defence - use Canadian spelling. This was noted in other parts of the document as well.
- ES-2.0, paragraph 2, 4th bullet - "include" should be "included"
- ES-7 - Dioxins "Many of the people exposed for a short time could have experienced elevated short-term health risks", i.e., this is describing something which occurred in the past.
- Section 1.0 - Footnote 1, page 1: there is an extra parenthesis in front of PCDFs.
- Section 1.0 - Page 2: "This report is organized as follows.....Section 2.0: Description of Tier 1 ~~Issues~~"
- Page 4 - 5th paragraph: "A system of time runs was used during application....."
- Page 5 - 5th paragraph: "40 km"
- Page 6 - 1st paragraph: typo - "hcbcontaminant"
- Figure 4-1 - 2nd footnote, typo "areaas"
- p. 19: 3rd paragraph, missing word: "This was accomplished *by* Army personnel..."
- p. 25: "t = aamount....."
- p. 32, 1st paragraph: "39 plots"
- p. 32, 2nd paragraph, 3rd line: "....with PCDD while and additional 18 plots were sprayed..."
- p. 35, 2nd paragraph: ".....rate prior to reaching a flagger."
- p. 35, 3rd paragraph: "....including ~~an~~ upper, lower and central approximations."
- p. 59 - 1st paragraph - "In particular...in another study of..."
- references - WHO. 2001. -typo: "Roam"

CANTOX ENVIRONMENTAL – RESPONSE TO PEER REVIEW AND HEALTH CANADA COMMENTS

Unless otherwise noted, all comments have been addressed.

Responses to comments made by the Peer Reviewers		
Section	**Major Comment**	**Response**
Major Issues 1) Exposure Estimates	*Issue:* From our perspective, there does not appear to be enough information provided to arrive at the same exposure estimates that are reported in Tables 5-12 to 5-17. We have tried to verify the estimated exposures in "ng/kg bw" and have not been able to arrive at the same values. More specifically, when we completed the exposure calculations using the supplied information, we arrived at different exposure estimates...	All exposure estimates have been reviewed and verified. A complete worked example has been appended to the report (Appendix E) that will allow the reader to follow all assumptions and calculations.
2) Background Exposure Estimates	Issue: An article by Lorber (2002) has suggested that average background dioxin-TEQ serum lipid concentrations in the US were between 50 ppt and 80 ppt during the 1970's whereas Cantox has used a value of 21.8 ppt. It is unclear if the Lorber paper is more accurate than the Cantox estimate and/or perhaps included other considerations. Nevertheless, if the Lorber value was used in the assessment, it is possible that appreciably different results would have been found (e.g., values in Table 7-1 would need to be revisited).	The Lorber (2002) paper has been reviewed and included in the revised assessment. Background exposure estimates for the 1960s have been revised to better reflect the situation at the time.
Major Issue 3) Inclusion of Dioxin-Like PCBs in Background Exposure Estimates	*Issue:* Somewhat related to the above, it is possible that dioxin-like PCBs may have contributed to the typical background exposures that receptors may have been receiving at the time of the spraying events. In some cases, dioxin-like PCB exposures may contribute appreciably and, thus, should possibly be considered or discussed in the Cantox report.	Discussion of dioxin-like PCBs was included in Appendix C whenever possible. Dietary intake of dioxin-like chemicals has been shown to contribute ~95% of an individual's daily dose. Estimates of dietary intake obtained from the Total Diet Study (Cao *et al*., 2005) included dioxin-like PCBs. In many cases the concentration of dioxin-like PCBs in environmental media (air, soil, and water) was not available. In one instance dioxin-like PCBs were evaluated in Canadian air. However, these compounds were found at significantly lower concentrations than the PCDD/PCDFs and were not included in the background air concentration. Therefore, dioxin-like PCBs are not believed to significantly contribute to dioxin like compound

Responses to comments made by the Peer Reviewers		
Section	**Major Comment**	**Response**
		exposure through environmental media.
4) Risk Calculations	Issue: If exposure estimates are found to require recalculation, then the Cantox risk estimates provided in Tables 7-2 to 7-24 and Figures 7-1 to 7-5 may need to be revisited. Currently, the risk estimates are reproducible only if the exposure estimates presented in earlier tables are accurate.	Further to comment 1 above, all exposure and risk calculation have been verified and modified as necessary.
5) Discussion	Issue: Stakeholders, health officials, and policy makers will want to know how these risks compare with those experienced by individuals in other cohorts, such as victims of the Seveso accident, industrial workers who made herbicides, agricultural workers who sprayed herbicides, or U.S. Air Force veterans of Operation Ranch Hand, the unit responsible for spraying Agent Orange and other herbicides in Vietnam.	This information has been provided.
6) Executive Summary .	Issue: Many readers will immediately look for the bottom line (on page ix) and will seek confirmation that the overall interpretations in the Executive Summary are consistent with material presented later. As currently written, the executive summary on page ix is not written with as much conviction as the bulleted items on pages 92 and 93	The executive summary has been modified to reflect this concern as well as other issues required revisions.
5.4.1.1, Page 29	Section 5.4.1.1, Page 29: The equations presented on this page uses several parameters for which it is hard to determine which values were actually selected for use by Cantox. Specifically, the following parameters were not easily defined when we attempted to confirm Cantox's calculations:	All comments relating to exposure equations and the inability to follow specific calculations have been addressed through the modification of Section 5.0 and the development of Appendix E (a worked example). This appendix provides all the input data and equations used in the modeling process. An exposure calculation example has been provided for each receptor group.
Table 5-9 and elsewhere	The Cantox evaluation has been based on data that is specific to the general population (both sexes). If it is known that only men were using the area, it may be possible to revise the assessment based on male-specific data. Since Health Canada (2004) obtained much information from Richardson (1997) (which provides data for male, female and both sexes combined), it may be a relatively straightforward approach to base the risk assessment on male-specific endpoints. It should be stressed, however, that we have not been provided with any information that suggest only males were present.	DND has provided the following in response to this question: *In order to determine whether women were involved in the trials, it would pay to look at the role of women in the Canadian Forces at that time. I believe that they were established in administrative roles only at that time, and would not have had active roles in either service support or combat trades and thus have limited to nil access to the training area and the spray program. Certainly there could be exceptions to the rule but that would be difficult to determine. We have no way to confirm whether women were involved or not as we simply don't have a list of persons involved in the 1966/67 program or thereafter either.*

Responses to comments made by the Peer Reviewers		
Section	**Major Comment**	**Response**
Section 5.4.5, Page 38	Perhaps the berry consumption rate could be provided as the number of servings per week.	This consumption rate cannot practically be expressed as the "number of servings per week". This consumption rate represents the average daily intake of wild berries over the course of the entire exposure duration. It is likely that consumption would not have occurred everyday but rather on a sporadic or opportunistic basis.
Section A1-1.0 Pentachlorophenol	Page A-1, paragraph beginning "According to the …". This is a nice calculation, leading to the conclusion that PCP was applied as a salt rather than as water insoluble PCP. To help the reader follow this more readily, please add the phrase "or, equivalently, 4 lb/gal" to the end of the third sentence.	The suggested change has been made and the basis of the calculations clarified
	Table A1-1.3, Page A-3: It is unclear how the mean values were derived. It is recommended that 2 or 3 significant figures be reported in the table.	The use of significant figures (three places) have been included in the Tables despite the fact that the numbers presented originally were as reported by the authors.
	Page A-4, paragraph beginning "In 1971, Elvidge …". Is it "Bionetics" or "Biometrics"?	The reference that appears in Elvidge is to Bionetics.
Section A2-1.0 Hexachlorobenzene Contaminant Levels	Page A-10, paragraph beginning "Technical grade picloram …", last sentence" Replace "in the 200 region of 200 ppm" with "in the region of 200 ppm".	The change has been made to reflect the comment
Page B-35, paragraph beginning "U.S. EPA (2004b)…", second sentence	Page B-35, paragraph beginning "U.S. EPA (2004b)…", second sentence: Replace "$(mg/kg/day)^{-1}$" with "$(mg/kg/day)^{-1}$". The narrative in this paragraph is further complicated by a recent paper that shows an increased all-site cancer risk with dioxin in Air Force Health Study control subjects, nearly all of whom have background dioxin levels; see Pavuk M, Michalek JE, Schecter A, Ketchum NS, Akhtar FZ, Fox KA. Did TCDD Exposure or Service in Southeast Asia Increase the Risk of Cancer in Air Force Vietnam Veterans Who Did Not Spray Agent Orange? *Journal of Occupational and Environmental Medicine* 2005;47(4):335-342.	This study has now been referenced in the report. "A recent paper by Pavuk et al. (2005) suggests that dioxin exposure is associated with an increase in all-sites cancer risk although the issue of a low-dose mechanism remains unclear."
Appendix D Page D-5, top line.	The conclusion of this commendable effort to validate the application of PHED data is understated. In fact, the results, as evidenced by skin 2,4-D levels in Table D-2, are consistent with the estimated exposure levels by receptor category described in Tables 5-12 through 5-17, indicating that the mixer/loader receptor had exposures at least an order of magnitude greater than the flagman receptor. This information should be added to the summary paragraph on page D-5.	Health Canada has provided further details regarding PHED; this information has been provided as part of Appendix D.

Responses to comments from Health Canada		
Section	**Major Comment**	**Response**
Page 4, 4th paragraph:	Text read ".....each plot received a series of four passes....". This contradicts the assumption used in the spray drift report where a single spray line with a 100 feet spray swath was assumed, as the report did not specify. Please clarify the discrepancy.	We believe this to be correct based on information provided by Demaree and Creager.
Section 2.0 Page 5/6	In the published literature, HCB is identified as a contaminant of PCP and should be assessed as such. See comments for Appendix A.	We were unable to locate any evidence of this in the published literature.
Section 5.3.1	Section 5.3.1 It is unclear how it was decided which parameters would be estimated as single values and which would be represented by a range (high, low, central estimates). This is basically introducing probability into some variables and not into others. The report authors should indicate if all the variables were examined systematically to decide which should be treated stochastically (as a data distribution) and which to be treated deterministically (as a single point estimate), with consideration to which are driving the risk. A logical step in this process would be some sort of sensitivity analysis, i.e., considering the effect on the results of varying the parameters over their expected ranges, to determine which parameters are most important.	We disagree with the reviewers general statements regarding the use of probability factors. We have not conducted a stochastic assessment which incorporates pre-defined probability density functions (PDF). The purpose of the 'low', 'central' and, 'high' point estimate exposure values was to provide a general appreciation for the inherent uncertainty and variability present when attempting to quantitatively reconstruct historical exposure events. Much of the site-specific and receptor time/activity patterns data are inadequate to develop meaningful PDFs. Providing a low, central and, high exposure estimates facilitates a semi-quantitative sensitivity analysis. Typically a sensitivity analysis is useful in identifying those input parameters which have the greatest influence on final exposure predictions. By identifying key input parameters, further data can be collect in an attempt to reduce the level of uncertainty in the overall exposure estimates.
Section 5.3.1.2 - Dermal Absorption	There are many published studies in which dermal absorption of dioxins was evaluated (e.g .those listed below). The results of these studies could be considered as part of a weight-of-evidence approach, by comparing measured and modelled values, to electing dermal absorption values for the low, central and high exposure estimates. Consider for example…	Based on a review of several different methods, the approach provided by the U.S.D.A. Forestry Service and SERA were considered most appropriate. It was felt that the review provided in the Appendix A was adequate.
Section 5.3.2 - paragraph 2	The incorrect conversion factor is cited for converting application rates from g/m2 to lbs/acre. The conversion factor cited is 1.12E-01 whereas the correct conversion factor is 8.9. This suggests that the exposure estimates could be underestimated by factor of approximately 80 times. Unfortunately, sample calculations were not provided to verify whether this error actually occurred in the calculations. Please verify that the correct conversion	This is an incorrect interpretation of the wording provided in the draft report. The correct conversion factor was used. This can be verified though examination of the Worked Example provided in Appendix E. This text has be modified to ensure clarity.

Responses to comments from Health Canada		
Section	**Major Comment**	**Response**
	factor was used in the calculations	
Tables 5-2, 5-3, 5-4 and 5-5:	Diesel is listed in Table 5-2 as a component of the applied mixtures but is not further addressed in the report. Is the intent to address this in the other tiers or to develop a rationale for its exclusion from the assessment?	As indicated in the scope of work, Tier I was concerned with two contaminants only.
Section 5.4.2	It would be useful to cite Technical Memorandum 141 (which identifies that one pilot applied all mixtures in about 30 hours of actual flying time over the three consecutive days, but does not identify the number of personnel involved in mixing and loading, or the number of flagmen.) Assumptions beyond what is actually known should be justified.	Noted, however, our assumption of applying all herbicide mixtures potentially contaminated with PCDD within one 12-hour day is considered reasonable. It is also in-line with the total number of hours spent spraying.
Section 5.4.1 and 5.4.1.2	The 30% clothing penetration rate applied here is not consistent with the 75% clothing protection factor used elsewhere in the report.	In the development of the PHED UEs, coveralls are assumed to provide a 75% protection factor for arms, chest, back, thighs and lower legs. This assumption was inherently accepted with the use of the PHED UEs in the routine exposure scenario for the mixer/loader (as well as other scenarios involving the use of PHED UEs). To be conservative, an additional exposure event was included in the risk assessment in which the mixer/loader was assumed to have a one-time accidental spill of 0.5 L of herbicide concentrate. Calculation of exposure resulting from this event was based on the methodologies recommended by ENSR (2005) in which a clothing penetration rate of 30% was used. Since this methodology was developed to address the specific scenario in which a given amount of herbicide concentrate was spilled on clothing, it was considered to be most appropriate to adopt this value for the current assessment. Since a more detailed description of the nature of the "protection factor" described in the PHED database was not available, it was not possible to ascertain whether this value was appropriate to use to assess a situation in which a significant amount of liquid was applied to the coveralls.
Section 5.4.3.2	Why was the factor of 2.7 chosen rather than the peak factors calculated by REMSpC's modelling? It is misleading to state that the factor of 2.7 is "based on an analysis provided by REMSpC" as it could be concluded that 2.7 was the peak factor from the modelling, when in fact 2.7 is from a 1964 report on calibration trials. The modelling predicted lower peak factors, i.e., Fig. 1 shows 1.4 for the 1966 trials and Fig. 2 shows around 0.85 for the 1967 trials. Similarly, the definition of 2.7, following the equation, as "worst-case multiplier based on wind speed and direction" suggests site-specific data and modelling	The wording in the main report has been changed to reflect this concern. However, a value of 2.7 was maintained. As the reviewer points out limited modeling was conducted, the results of which indicated the 1967 trials (which were limited relative to the 1966 campaign) could produce application rates 1.4 times the intended rate. Given the uncertainty here, the risk assessment fell on the side of caution and employed the value from the actual 1964 calibration trials.

Responses to comments from Health Canada		
Section	**Major Comment**	**Response**
	were used to generate this factor, which is not the case.	
Section 5.4.4	As noted in the Statement of Work for this contract, PMRA has produced a guidance document on the principles/theories of estimating potential exposure using dislodgeable foliar residue (DFR) data and agricultural transfer coefficients (TCs) for estimating potential exposure to people entering areas treated with pesticides, including areas similar to forestry scenarios (Post-application Exposure Monitoring Test Guidelines (PRO98-04) available at http://www.pmra-arla.gc.ca/english/pubs/pro-e.html). Additional information on this topic is generated by Exposure Task Forces and can be found at: www.exposuretf.com and on the websites for PMRA and the U.S. EPA. Cantox estimated exposure to the field scout using a method developed by the USDA Forest Service. It would be useful to include a discussion in this section of the USDA exposure assessment methodology versus the standard methodology used by the PMRA and the U.S. EPA, including what are the strengths and weaknesses of both approaches, inherent conservatism and uncertainties, and validation and acceptance of both methods. Also discuss how the transfer rates are derived for both methods and whether it is validated based on actual data.	The general Statement of Work request that a human health risk assessment be completed. Although a full literature review of all the different approaches and methodologies used by various agencies would be of interest, it was not considered part of the modified Tier I scope. The current assessment has not used an out-dated methodology but one currently used by the U.S.D.A. Forestry Service. If the review feels that a thorough review of all approaches relative to one another is necessary, this could be included (as an expanded scope) for another Tier.
Section 5.4.5	Military Trainees *"Military trainees were assumed to spend 2 months of the year at the 1966 spray campaign site."* It is unclear what this assumption is based upon, and whether this is an average estimate, or is it longer than average, i.e. conservative.	As indicated in each parameter table, this exposure parameters was assigned a single point-estimate value of 2 months. It was assumed that a trainee could spend up to 2 months of the year training in the area of the 1966 or 1967 spray campaign. There was not enough site-specific information to clearly define what is considered an average versus a conservative estimate.
Sections 5.5.1 - 5.5.3	Based on the manner in which the equations and data are presented in the report, the calculations cannot be verified. Many of the equations in the report are difficult to understand as the units do not cancel. Inputs for the equations are not readily available; the reader has to search through the report and find some of these inputs in the appendices.	All comments relating to exposure equations and the inability to follow specific calculations have been addressed through the modification of Section 5.0 and the development of Appendix E (a worked example). This appendix provides all the input data and equations used in the modeling process. An exposure calculation example has been provided for each receptor group.

Responses to comments from Health Canada		
Section	**Major Comment**	**Response**
Section 6.2.5 Body Burden of Dioxin and 7.2.5 Dioxin Body Burden Calculations	The whole weight blood values described in section 6.2.5 from the CDC survey should be in fg/g units and not pg/g.	We don't believe this to be correct, please see Table 93 in CDC (2005).
Section A1-1.0 Pentachlorophenol	The following Canadian reviews on pentachlorophenol and its contaminants should have been consulted during the preparation of these comments, to obtain additional data sources for levels of impurities in PCP formulations: -Jones, P.A. (1981). Chlorophenols and their Impurities in the Canadian Environment. Report EPS 3-EC-81-2, Environment Canada, 434 pp. -National Research Council Canada.. 1982. Chlorinated phenols: Criteria for environmental quality. NRCC No. 18578. 191 pp. -Gilman, A.P.; Douglas, V.M.; Newhook, R.C.; Arbuckle, T.E. (1988) Chlorophenols and their impurities: a health hazard evaluation. Health and Welfare Canada.. Document No. H46-2/88110E. Based on the above reviews, additional dioxin levels in American PCP products, should be provided and considered for the exposure and risk assessments. For example, papers from Rappe et al (1982), Nilsson et al, (1978), Rappe et al (1978), Rappe et al (1979) and Arsenault et al (1976) all contain such information.	In Jones (1984) it states that Agriculture Canada identified the phenolic impurities in PCP and NaPCP. In 14 samples of technical PCP from five suppliers two isomers of DCP, three isomers of TCP and three isomers of TTCP were reported. Based on percent content, the major impurities were 2,4-DCP; 2,3,5,6-TTCP and 2,3,4,6-TCCP. In three samples of NaPCP from one supplier the only major impurity was 2,3,4,6-TTCP. Concentrations of dioxins were not reported for these samples. **CEI response**: Jones (1984) does not provide data on PCDD/PCDF in technical grade PCP such as Timbertox Jones, PA (1981) concluded that " the identities and quantities of imputrities (PCDDs and PCDFs) in higher chlorinated phenols in Canadian products and in products imported from Europe are not well documented in contrast to the information on impurities in chlorophenols produced in the U.S. (Sect. 3.1)" Jones (1981) also concluded that "some PCP imported from Europe had been produced by alkaline hydrolysis of hexachlorobenzene (HCB) and, therefore, contained HCB as an impurity (Sect 2.1)." **CEI response**: The product used in 1967 (Timbertox) was manufactured in the U.S. It was concluded that this product had no HCB contamination. The purpose of the monograph produced by the NRC (NRCC 18578 (1982)) was to "provide an analysis of the scientific criteria as well as research recommendations that were specific to the chlorophenols and not to the PCDDs *per se*." This document (and its appendices) does not provide any significant information on PCDD/F contamination in PCP, but focuses primarily on the chlorinated phenols themselves as sources of contamination and adverse effects on the environment. **CEI response:** NRCC 18578 does not provide any useful information on specific congener concentration for polychlorinated dibenzo-*p*-dioxins or dibenzofurans in PCP. *Chlorophenols and Their Impurities: A Health Hazard Evaluation*. Health and Welfare Canada.. Document No. H46-2/88110E (1988) provides a summary table (Table 3, page 15) that reports the data from Rappe *et al.,* (1979) which we have cited in the document as one of the sources of information on dioxin

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		contamination in PCP. No other information that explicitly addresses the concentration (range or quantification) of PCDD or PCDF in samples of PCP are provided in the document. The dioxin data for the "American sample" of PCP has been entered into Table A1-1.1 **CEI response**: Data for the "American product" was entered into TableA1-1.1. This single sample altered the mean $\sum TEQ_{WHO}$ upwards to 9.245 and changes the range to ~45 ppm TEQ. Rappe et al (1978): Identification of polychlorinated dibenzofurans (PCDFs) in commercial chlorophenol formulations. Chemosphere 12: 981-991. Data in this document provides concentration data (one sample) for dibenzofurans PCP. **CEI response:** The data in this paper is similar to that reported in Buser and Bosshardt, 1976 which is one of the sources of information already described in Table A1-1.1 and used to generate the $\sum TEQ$ for use in the assessment.
	The main report text needs to reference this appendix where appropriate	Reference to this section of Appendix A has been made in the Main Report
	Page A-1, para.. 1, last sentence states: "The use and uncontrolled incineration of technical grade PCP is one of the most important source (typo, singular) of PCDDs and PCDFs in the environment". Please provide reference for this statement. This statement may have been true at one time in the past but the current uses of PCP are strictly limited to industrial uses (heavy duty wood treatment). Reference: Agriculture Canada.. 1992. Re-evaluation of heavy duty wood preservatives. Announcement A92-02. Available at: http://www.pmra-arla.gc.ca/english/pdf/rev/rev_a9202-e.pdf)	The purpose of the review is to discuss the relevance to human health of the use of technical grade PCP used at the time (1967); therefore this sentence has been changed to past tense. Reference has been made to revised manufacturing practice and controlled use. Incineration of PCP: reference Karasek FW, Dickson LC., 1987. This reference appears in the text
	Page A-1, para. 5 states that: "The water soluble form of PCP (pentachlorophenate salt) generally had lower concentrations of PCDDs and PCDFs when compared to organic soluble pentachlorophenol. However, Table A1-1.1 clearly shows that detectable amounts of TCDDs (0.05-0.25ppm) were ONLY found in Na-PCP samples. This is also contrary to the statement below table A1-1.1 : "These reports all agree that the lower substituted congeners (....) were below the detection limit. These unexpected results were later found to be an unusual 1,2,3,4- substituted isomer (Buser and Rappe 1978 in: Rappe et al 1982).	The text has been revised as suggested to point out that organic solvent soluble PCP exhibited low levels of tetra- and penta-chlorodioxins. The suggested explanation of the elevated concentrations of tetrachloro-dioxins in NaPCP has also been adopted.

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	Page A-2, Table A1-1.1. In the title, please replace the term "commercial" by "commercially available". Commercial grade PCP was a formulation that contained up to 20% tetrachlorophenol, a product very different from the technical grade PCP that was available at the time (REF).	The Table title has been changed
	Page A-3, Table A1 1.2, title, as above	The Table title has been changed
	Page A-3, Table A1 1.3. Title: please change to .... based on Tables A1-1.1 and A1 1.2	The change has been made
	Page A-3, Table A1 1.3. The values in the min and max rows are inverted	The error has been corrected
	Page A-3, Table A1 1.3. last row: "Total ppm by TEF" should read : Total ppm as WHO-TEF	The values have been changed and express TEQ according to WHO (TEQ_{WHO})
Section A1-2.0 2,4,5-Trichlorophenoxyacetic Acid (2,4-T)	Page A-4 states "one sample of 2,4,5-T contained about 27 ppm..." but Table A1-1.4 reportedly citing the same study (Elvidge, 1971) does not list any TCDD concentration greater than 0.50 ppm. Additional information is provided by Firestone et al (1978) who reported levels of 2,3,7,8-TCDD in stored drums of Agent Orange (before 1970), and estimated levels as high as 100 µg/g (100 ppm) in individual 2,4,5-T formulations	The Table A1-1.4 is correct. The text has been changed to show 0.27 ppm, not 27 ppm. The content of TCDD in Agent Orange used in the report has been changed to include a range of concentrations as indicated by Young, 1980. This range was based on nearly 500 samples of AO from unused material that remained unused in the US military at the end of the Viet Nam conflict. It was believed that this analytical data was representative of the likely content of TCDD in Agent Orange, and does not represent an "estimate".
	Page A-6: para. 4: Edmunds et al (1973) in not cited in the reference section	The reference has been included.
	Section A1-2.1 Agent Purple, Page A-6: It seems very probable that the dioxin level (45 ppm) reported by Young *et al.* (2004) in a single agent purple sample would be referring to the same sample reported earlier as 45 ppm TCDD by the same author. Please verify. The "Detrick" reference is not cited in the reference section	The references by Young in 1980 and 2004 (a review) are to the same sample of Agent Purple. The reference to reports from Fort Detrick were made by Young, so there is no need to refer to them separately.
	Page A-6: Agent Orange weighted mean concentration of TCDD was 1.98 ppm.But the maximum detected was 15 ppm, so using 2 ppm is not a worst case, i.e., the TCDD content could have been higher. Why was a range used for Agent Purple and not for Agent Orange, when there are data on the range measured in Agent Orange?	A range of concentrations of TCDD in Agent Orange (<0.02 to 15 ppm) has been used on the revised risk assessment calculations.
	Page A-7 states "For the purposes of the current assessment all 2,4,5-T in Agent Purple should be assumed to be contaminated at a level of 45 ppm TCDD." In the report, however, a range of 5 to 45 with a central estimate of 32.8 ppm is used.	

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	Report text needs to reference this appendix where appropriate.	References to the Appendix have been made in the text of the Main Report.
Section A1-4.0 Conclusion	No comments were made but as clarification of the quantities used in the risk assessment the summary of conclusions has been included here.	Each contaminant has been assigned a range of concentrations of TCDD or TEQ_{WHO} in the conclusions for the concentrations to be used in the current assessment. These are: 2,4,5-T (isobutyl ester and butyl ester) in Agent Purple should be assumed to be contaminated at a level of 45 ppm TCDD with a range of 5 to 45 ppm TCDD. 2,4,5-T (butyl ester) in Agent Orange should be assumed to have a level of contamination by TCDD of 2 ppm with a range of 0.02 to 15 ppm. All other products that contain 2,4,5-T as the phenoxyacetic acid (Labelled in the DND documents as "Other" and "M-2993") the level of contamination by TCDD is assumed to be 2 ppm [range of 0.02 to 15 ppm]. The level of TCDD contamination (as determined by TEQ) in PCP applied in 1967 is 9.242 ppm with a range of 2.154 to 45.010 ppm TCDD (TEQ_{WHO}).
Table B1-2, Chem/Phys properties of TCDD:	Many of these values are different from those in Task 2A, Table A-1, which were supposed to provide a common database for all other tasks. The two sets of phys/chem values should be reconciled.	Values have been cross-checked to ensure consistency. However, it is noted that recent references have been used in some instances.
	1) TCDD half-life in soil is listed as 10,000-30,000 hours, which converts to a range of 1.1 to 3.4 years. What is the value in parentheses - an approximate mean? 2) The half-lives in soil vary over a wide range; was this range reflected in the exposure assessment calculations of soil concentration 1 year after spray event (p. 38), or was a single value used? It is unclear where the values were used. Using the low end (10,000 hours), the fraction remaining after 1 year is 0.54, while using the high end (30,000 hrs), the fraction remaining after 1 year is 0.82. How sensitive is the risk estimate to this range?	1) Values listed are the range and the mean (in parentheses). All values have been corrected and additional information added to the table. 2) Refer to Table 5.13 in the main report. A range of environmental half-lives, determined using JW, 2006 and Mackay et al., 1992, were utilized in the exposure assessment. The half-lives utilized were 1, 2, and 3 years for the low, central and high values, respectively.
	Half-life in sediment water is listed as >30,000 hours. This converts to 3.4 years, which does not match value in parentheses (~6 years).	Values have been corrected: Sediment water: Range: >30,000 h; Mean: 55,888 (~6 years)
	Text on page B-37 states that half-lives in soil and sediment range "from 2 to greater than 6 years". Not consistent with Table B1-2, which has 1.1-3.4 yrs for soil, and >3.4 years for sediment.	Text has been changed so that the values are consistent.

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Table B2-2.1: Chem/phys properties HCB	Values are different from those in Task 2A, Table A-1.	Values have been cross-checked to ensure consistency. However, it is noted that recent references have been used in some instances.
	Half-lives in soil in table are referenced as Mackay et al. 1992, but half-lives in soil on page B-76 are referenced as Griffin and Chou, 1981.	Half-lives from other scientific studies are presented on page B-76, along with those values determined by Mackay et al., 1992 and JW, 2006. The values of Mackay et al., 1992 and JW, 2006 are the only values presented in the table as they are the soil half-lives utilized for modeling within this risk assessment.
Page B-17, para. 2	"In an NTP study completed in 2003 (NTP, 2004a, b, c, d)...". Four references are listed. Which is the correct one?	References have been corrected. In some instances all of the references were appropriate; while in others the correct reference was selected.
Page B-17, para. 3	Again 4 references are listed. Which is the correct one?	
Section B1-4.1 Absorption	Most of the references in this section are quite old. Please provide more updated information and revise text.	Additional references were added to this section. These included: Nolan, R.J., Smith, F.A., and Hefner, J.G. 1979. Elimination and tissue distribution of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in female guinea pigs following a single oral dose. Toxicol Appl Pharmacol 48(1):A162. Cited in: U.S. EPA, 2003. Olson, J.R., Gasiewicz, T.A., Neal, R.A., *et al*. 1980. Tissue distribution excretion, and metabolism of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the Golden Syrian Hamster. Toxicol Appl Pharmacol 56:78-85. Cited In: ATSDR, 1998. Poiger, H., and Schlatter, C. 1986. Pharmacokinetics of 2,3,7,8-TCDD in man. Chemosphere 15: 1489-1494. Cited In: Edmond *et al.*, 2005. Birnbaum, L.S., and Couture, L.A. 1988. Disposition of octachlorodibenzo-p-dioxin (OCDD) in male rats. Toxicol Appl Pharmacol 93:22-30. Cited in: U.S. EPA, 2003. Umbreit, T.H., Hesse, E.J., and Gallo, M.A. 1986a. Bioavailability of dioxin in soil from a 2,4,5-T manufacturing site. Science Report 232:497-499. Umbreit, T.H., Hesse, E.J., and Gallo, M.A. 1986b. Comparative toxicity of T_4CDD contaminated soil from Times Beach, Missouri, and Newark, New Jersey. Chemosphere 15:2121-2124. Cited In: Shu *et al.*, 1988. Nessel, C.S., Amoruso, M.A., Umbreit, T.H., *et al*. 1992. Pulmonary bioavailability and fine particle enrichment of 2,3,7,8-tetrachlorodibenzo-p-dioxin in respirable soil particles. Fundam Appl Toxicol 19:279-285. Cited

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		in: U.S. EPA, 2003. Brewster, D.W., Banks, Y.B., Clark, A.M., *et al*. 1989. Comparative dermal absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin and three polychlorinated dibenzofurans. Toxicol Appl Pharmacol 97:156-166. Cited in: U.S. EPA, 2003. Banks, Y.B., and Birnbaum, L.S. 1991. Absorption of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) after low dose dermal exposure. Toxicol Appl Pharmacol 107:302-310. Cited in: U.S. EPA, 2003. Weber, L.W.D., Zesch, A., and Rozman, K. 1991. Penetration, distribution and kinetics of 2,3,7,8-TCDD in human skin in vitro. Arch Toxicol 65:421-428. Cited in: U.S. EPA, 2003.
	Page B-21, 1st para. It is surprising to find an MOE (1985) reference to provide such information. Please use more appropriate recent references.	It is unclear as to why the MOE Scientific Criteria Document for Standard Development for polychlorinated dibenzo-*p*-dioxins (PCDD's) and polychlorinated dibenzofurans is not considered a relevant reference. Other recent references were added, where appropriate, to support the adsorption rates for dioxin-like compounds via ingestion and dermal contact as cited by the MOE.
	Page B-22, para. 2 and 3: Please provide references for those 2 paragraphs as it is unclear if all the information presented here is from Dann (1989)	Sections were omitted in the revised report.
Page B-76:	HCB half-lives in soil vary over a range; was this range reflected in the exposure assessment calculations of soil concentration 1 year after spray event (p. 38)? The values could not be located	Refer to Table 5-13 in the main report. A range of environmental half-lives, determined using JW, 2006 and Mackay et al., 1992, were utilized in the exposure assessment. The half-lives utilized were 2.7, 6, and 7.5 years for the low, central and high values, respectively.
Appendix C Major Comments	1)An average daily intake estimate of PCDD/DFs and dioxin-like PCBs via food consumption specifically for adults has not been calculated to estimate current exposure levels. Instead, the present day average exposure estimates of PCDD/DFs and dioxinlike PCBs through food consumption are given in the form of just one value, “0.88 pg TEQ/kd/day” for all Canadians (all age groups and genders combined) from the Total Diet Study (1992 to 1999). This mean value, calculated by the Food Safety Division, comprised all the individual daily food intake rates from all the respondents from the	1) The value is no longer inappropriately represented as a lifetime EDI weighted by age. 2) Although it is true that only adult receptors are considered in this risk assessment, individuals would have experienced dioxin exposure both prior to and following any exposures experienced at Gagetown. Due to the long body half-lives of dioxin-like compounds utilizing a lifetime average is appropriate as it captures both early and late life stage exposure. 3) Information of this nature was considered beyond the scope of the current study. Information is readily available from other sources.

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	Nutrition Canada Survey (1970-1972) that were combined the respective contaminant levels in each of the analysed food composites (Personal communication from Dr. Xu-Liang Cao, Food Research Division, Bureau of Chemical Safety, Health Products and Food Branch, Health Canada). The resulting EDI, "0.88 pg TEQ/kd/day", is the overall mean calculation for all individuals, regardless of age or gender. It is not a calculated lifetime EDI weighted by age as inappropriately presented in Tables C1-1.6 and C1-1.7. 2)It was unclear why a lifetime composite receptor was used instead of the adult, as only adult receptors are considered in this risk assessment. 3) In addition, more background information on the Total Diet Study and the Nutrition Canada Survey should be provided in this Appendix (see Cao, 2005).	
Major Comment related issues	Therefore, adult age-specific DLC (dioxin-like compounds?) intake estimates should be calculated using a complete set of data on levels of DLCs detected in analysed food commodities from the Total Diet Study (1994-1995 and 1995 to1999). These latter, more recent concentrations of DLCs were provided to Mr. Elliot Sigal of Cantox Environmental Inc. on January 5, 2006 by Ms. Deborah Schoen of Health Canada regarding Cantox (2006). These data were obtained in a personal communication from Dr. Jake Ryan (Senior Research Scientist, Food Research Division, Bureau of Chemical Safety, Health Products and Food Branch, Health Canada). Please contact Health Canada to obtain these data sets if they are currently unavailable.	Adult age-specific DLC intake estimates were not calculated as a lifetime receptor was utilized in the risk assessment (see above). Therefore, the average dietary intake value of 0.88 pg TEQ/kd/day for all Canadians (all age groups and genders combined) from the Total Diet Study (1992 to 1999) is appropriate to determine the current EDI rate.
	For the background values for the other exposure media (air, water and soil) please provide additional information on the data sets: dates, types of surveys, complete references, etc.... In addition, provide a discussion on how representative the historical EDI represent the exposure in 1966 and 1967 or if it is more representative of another time period?	Additional background information was added for each environmental media (air, water, soil, consumer products). The following paragraph was added to discuss what time period the environmental data was most representative of. "The studies used to estimate historical levels of dioxins, furans and dioxin-like PCBs in Canadian environmental media were conducted between 1990 and the present day. This is partially due to the low detection limits required to detect these particular contaminants. In air for instance, the detection limits (pg/m^3) required to detect dioxin-like compounds were not achieved until the mid 1980s.

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		Therefore, the background PCDD/PCDF concentrations in environmental media (air, water, soil and consumer products) utilized to establish the Canadian current and historical EDI rates are representative of concentrations in environmental media between 1990 and present day. However, the historical EDI rates for dioxin-like compounds determined above (Table C1-11) are considered representative of historical exposures as in several instances, historical data from the early 1980s are consistent with the selected background environmental media concentrations. However, the majority (~95 to 97%) of exposure to Dixon-like chemicals for Canadians occurs through food consumption. Therefore, even large changes (ten fold) in environmental media dioxin, furan or dioxin-like PCB concentrations will not have a significant effect on the Canadian EDI rate."
	A review of previous Canadian exposure assessments to dioxins and furans has not been performed. What is the rationale for this data gap? A good starting point would the exposure assessments presented in the 1990 CEPA report. Other papers by Birmingham et al (1989a; b) and Ryan et al (1997) should also be considered.	This was conducted using Birmingham et al., 1989a,b and the 1990 CEPA report.
	Throughout this appendix, it is difficult to compare various estimated daily intakes as they are either reported as a daily intake (x pg/day) or on a body weight basis (x pg/kg bw/day), sometimes in the same sentence. Please report the intake data in a consistent manner.	Modified to be consistent.
	The notable downward temporal trend in the DLC concentrations in various environmental media, even during the last decade, should be presented and discussed, when possible. For example, consider presenting Figure 23 from Cao et al (2005) to show the trend over 8 years. For example, Lorber(2002) and Aylward and Hays (2002) provide empirical evidence of this downward trend.	The notable downward temporal trend was discussed when possible. Evidence was extracted from Cao et al., 2005, Lorber, 2002, and Aylward and Hays, 2002.
Historical Dioxin Levels	Page C-8, the last paragraph actually presents the results of a pharmacokinetic modelling exercise performed by Pinsky and Lorber (1998). The last sentence states: " This dose (1.5 to 2.0 kg/kg/day) may have dropped to as low as 0.1 pg/kg/day (7 pg/day) and less into the 1980s". How do you reconcile these estimated results with those presented in Table C1-1.10? The more recent modelling results from Lorber (2002) and Aylward and Hays (2002) would have	More recent modeling results (Lorder, 2002; Aylward and Hays, 2002) were discussed.

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	been much more appropriate.	
Section C2-1.0 Hexachlorobenzene (HCB) Estimated Daily Intake	The major comments (lifetime receptor, ...) outlined above for PCDD/DFs also apply to hexachlorobenzene.	Although it is true that only adult receptors are considered in this risk assessment, individuals would have experienced HCB exposure both prior to and following any exposures experienced at Gagetown. Due to the long body half-life of HCB utilizing a lifetime average is appropriate as it captures both early and late life stage exposure.
	This entire section is essentially based on the Priority substances list assessment report for HCB published in 1993. Cao et al (2005) is the only new reference added to this section. Please perform a literature review to identify new data sources to present a more current exposure assessment.	A literature review to provide a more current exposure assessment was considered beyond the scope of this assessment.
Health Canada Total diet Study	Table C2-1.2: it is incorrect to calculate weighted averages for HCB because the exposure varies according to diet age-specific diet. Please calculate arithmetic means for each age class based on the results presented in Table 10 from Cao et al (2005)	This was corrected.
General	Historical and Current HBC EDI - Table C2-1.5 is identical to Table C2-1.3: why was it necessary to present it again?	The duplicate table was deleted.