
Human Health Risk Assessment

Appendix 8

Statement of the Expert Peer Review Panel

Expert Peer Review Panel Members

The science of risk assessment, as it is used to evaluate the potential human health risks of exposure to environmental contaminants, is rapidly advancing. To ensure that the most recent and most appropriate science was used for the Rodney Street community risk assessment the ministry assembled an international expert peer review panel which included toxicologists and risk assessors from Canada, the United States and Norway. The panel members were selected on the basis of their extensive knowledge and international reputation in the areas of toxicology, risk assessment, and the health effects of nickel. Panel members included:

Dr. Ambika Bathija, United States Environmental Protection Agency, Washington, D.C., USA

Dr. Lynne Haber, Toxicology Excellence for Risk Assessment, Cincinnati, Ohio, USA

Dr. Robert Jin, Ontario Ministry of Health and Long-Term Care, Toronto, Ontario, Canada

Dr. Tor Norseth, Norwegian National Institute of Occupational Health, Oslo, Norway

Dr. Rosalind Schoof, Gradient Corporation, Seattle, Washington, USA

Dr. John Wheeler, Agency for Toxic Substances and Disease Registry (ATSDR), Atlanta, Georgia, USA

Statements of the Peer Review Panel

In August 2001 the panel members critically reviewed a working draft of the ministry's report. A professional facilitator was hired and a meeting of the panel members and ministry scientists was held in Toronto on September 20 and 21, 2001 to resolve issues raised by the panel's review. Follow-up teleconferences were held on October 16 and 19, 2001. The report was revised based on consensus decisions reached with panel members and the October 2001 draft report was placed on the EBR for a 30 day public consultation period. Following the September meeting and October teleconferences the panel members agreed to the following statement:

The draft document entitled *Soil Investigation and Human Health Risk Assessment for the Rodney Street Community, Port Colborne: October 2001*, and the report entitled *Recommendations and Conclusions from the International Expert Panel Meeting*, as received October 12, 2001, together with revisions addressing verbal comments tabled in the teleconferences held on October 16 and October 19, 2001, appropriately address the issues raised at the expert panel meeting held in Toronto, Ontario on September 20 - 21, 2001. Panel members also reviewed revisions to the October 2001 draft made as a result of the November 2001 public consultation period and concurred that the revisions and the ministry's response to the public comments were appropriate.

The ministry received twelve submissions on the *Soil Investigation and Human Health Risk Assessment for the Rodney Street Community, Port Colborne: October 2001* draft report as a

result of the 30 day November 2001 EBR public consultation period. The Environmental Bill of Rights Act stipulates that the ministry must take every reasonable step to ensure that all comments relevant to the proposal received as part of the public participation process are considered in it's decision (S. 35 EBR Act). Based on the EBR comments, the October 2001 draft report was revised and a summary of the public comments and how the ministry responded to them, was provided to the panel members in February 2002. The ministry asked the panel to review the report's revisions, the public comments, and the ministry's response to the comments. All panel members concurred with the following statement:

As an expert panel member for the Ontario Ministry of the Environment's Port Colborne human health risk assessment project, I have seen the final draft of the report, as provided to me under cover letter dated January 30, 2002, and I have reviewed the comments received by the ministry through their public consultation process. I concur that, where the changes to the report and the comments pertain to the science and expert judgement that guided the development and application of the risk assessment model, the ministry has responded appropriately. I have not been asked to, nor would I comment on or be expected to concur with, issues relating to how the ministry addressed public opinion or administered government policy.

Recommendations and Conclusions From the International Peer Review Panel Meeting

Meeting to Review the Draft Revised Human Health Risk Assessment of the Rodney Street Community completed by the Ontario Ministry of the Environment (MOE)

**Radisson Plaza Hotel Admiral
Toronto, Ontario, Canada
September 20 and 21, 2001**

The Ontario Ministry of the Environment assembled a panel of internationally recognized scientists to conduct a peer review of the ministry's draft report entitled *Soil Investigation and Human Health Risk Assessment for the Rodney Street Community: Port Colborne (Revised 2001)* (hereinafter referred to as the Revised 2001 HHRA Study). The Panel's recommendations and conclusions from the review of the study primarily focus on nickel, and are summarized in the following consensus statements.

Statement as to Conflict of Interest:

The members of the assembled International Peer Review Panel have declared they have no existing conflict of interest with respect to review of this assessment. They are not employed by, under contract to, or received monies from Inco with respect to the matter under review.

Overall Conclusion:

The International Peer Review Panel concluded that:

- In general, the methods followed in the study are consistent with the currently generally accepted risk assessment paradigm.
- The Panel supports the process and methodology as applied for the purpose of the Rodney Street assessment.
- A number of specific revisions were recommended by the Panel and are outlined below in this recommendations and conclusions document.
- The Panel came to consensus on the set of data and parameters which should be used for establishing a soil intervention level for nickel for the Rodney Street community.
- The available scientific data on dermal sensitization are inadequate to estimate a soil intervention level that would protect sensitized individuals from nickel dermatitis, or that would protect people from being sensitized to nickel.
- The additional analyses on nickel speciation and bioaccessibility conducted for the

Revised 2001 HHRA study improved the confidence and reduced uncertainties in interpreting the results of the assessment. This is a significant contribution to the site-specific risk assessment methodology for nickel.

Major Strengths Identified by the International Peer Review Panel

The following major strengths of the Revised 2001 HHRA Study were noted by the International Peer Review Panel:

- The methods described in the report of Revised 2001 HHRA Study provided a clear, easily followed outline of how the risk assessment process is currently used by regulatory agencies to develop intervention levels of chemicals and metals in various environmental media that are considered protective of human health.
- The multi-media, multi-pathway approach followed in the Revised 2001 HHRA Study was appropriate and clearly described.
- The speciation analysis of nickel appropriately evaluated the forms of nickel present in the community, and the implications of that speciation on nickel exposure in the risk assessment.
- The assessment of bioaccessibility/bioavailability of nickel from Rodney Street soils was properly conducted. The estimate of the relative bioavailability of soil nickel *versus* soluble nickel was accurately incorporated into the risk assessment.
- The Reference Dose (RfD) of 20 micrograms per kilogram body weight per day (US EPA) was considered to be appropriate and protective of human health.
- The Revised 2001 HHRA Study accurately demonstrated that oral exposure was the major exposure pathway of concern for nickel in soils and that inhalation and dermal exposure pathways had a minor contribution to the intake of total nickel from soils.

Action Items Recommended by the International Peer Review Panel

The International Peer Review Panel recommends that the following action items be addressed in the Revised 2001 HHRA Study:

1. Oral Toxicity and Exposure Criteria

- 1.1** There is uncertainty in the extrapolation to humans of effects arising from nickel exposure in laboratory studies, both in the concordance of endpoints and in the determination of appropriate intake criteria. These uncertainties, and the relevance to humans of the endpoints in animal studies should be discussed in greater depth.

Response: Addressed in chapter 6 (Part B, Main document) and Appendix 2 (section A2-1).

1.2 The Review Panel considers the US EPA RfD of 20 µg Ni/kg/day appropriate for use in this study. The confidence in this RfD was increased by the findings of a recent two-generation reproduction study where rats were exposed to nickel sulphate hexahydrate (Springborn, 2001). This study addresses a key data gap in the data used for the development of the current US EPA RfD value. A preliminary RfD of 20 µg Ni/kg/day based upon the Springborn (2001) study is under review by the US EPA. These issues should be discussed in the overall strengths and uncertainty analysis of the assessment.

Response: Addressed in Appendix 2 (section A2-9.2.2 and A2-9.3.2).

1.3 Some of the toxicological endpoints attributable to nickel in laboratory studies using animals (e.g., systemic effects on b and A2-body weight) have not been evaluated in epidemiological studies of workers exposed to high levels of nickel. However, some similarities have been observed in sensitive endpoints in both laboratory animals and humans (e.g., possible adverse reproductive outcomes in female workers in the nickel refining industry and in reproduction toxicity observed in laboratory studies in animals exposed to nickel). A discussion of these issues should be included in the uncertainties section in the revised document.

Response: Addressed in Appendix 2 (section A2-1).

1.4 The rationale for application of uncertainty factors typically used in risk assessment to establish regulatory exposure criteria would be most useful in the methodology section (Appendix 2). This documentation could then be referred to in the main text of the report, and in the discussion of strengths and uncertainties of the overall assessment.

Response: Addressed in Appendix 2 (section A2-1).

1.5 All the RfDs and equivalents are expressed as µg Ni/kg/day, so a conversion to nickel sulphate is not required for the TERA value. The text in the draft report should be modified appropriately to correct this issue.

Response: This issue has been addressed in the oral exposure limit sections of Appendix 2. However, due to the way inhalation exposure limits are described, it has not been addressed for those limits. This issue is being addressed.

1.6 The existing discussion of the rationale for different regulatory exposure values by various agencies (e.g., US EPA, Health Canada, WHO) should be expanded by adding information from the Springborn (2001) study, and develop an appropriate discussion of the rationale for the selection of criteria used in the MOE's assessment.

Response: Addressed in Appendix 2 (section A2-9.2.2 and A2-9.3.2).

1.7 It should be clearly stated in the uncertainty discussion (in addition to the discussion in Appendix 2) that the EPA definition of an RfD provides a recommended exposure criteria

estimate within an order of magnitude. This uncertainty impacts the degree of confidence in the selected soil intervention level.

EPA's IRIS database provides the following definition of an RfD: "In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime."

Response: Addressed in Appendix 2 (section A2-1).

2. Inhalation Toxicity and Exposure Criteria

2.1 It is recommended that inhalation risk estimates should be calculated and discussed using the EPA, WHO and Health Canada cancer potency factors for inhalation of nickel. This information will provide an estimate of the range in predicted risks based on current regulatory exposure criteria. It is important to indicate that the regulatory potency criteria are primarily developed to ensure the safety and the health of the public. The estimates of occupational exposures associated with cancers, as documented in various epidemiological studies, should be contrasted with the estimated inhalation exposures from the Rodney Street assessment. A discussion of this comparison is needed to provide a rationale for the conclusion that health risks from inhalation exposures based on the Rodney Street data are minimal.

Response: Addressed in section 5.6.2 (Part B, Main document) and Appendix 2 (sections A2-9.2.3.2 and A2-9.3.1).

2.2 The discussion in the uncertainty analysis of the cancer assessment, particularly in the estimates of exposure in the epidemiological studies used to derive the cancer slope factor, requires further discussion.

Response: Addressed in Appendix 2 (section A2-9.3.1).

2.3 Impacts of particle size on deep deposition of nickel into the lungs, resulting in higher tissue dose, requires expanded discussion. The cancer slope factor for nickel refinery dust is based on lung cancer, not nasal or total cancer. Therefore, a discussion of the issue of particle size and degree of penetration into the lungs is important.

Response: Addressed in Appendix 2 (section A2-9.2.1.1).

2.4 Using nickel concentrations in air expressed as TSP (total suspended particulate) rather than PM₁₀ (particulate matter less than 10 microns in diameter) is more appropriate because the cancer unit risk values are based on nickel refinery dusts of variable sized particles, including a significant fraction of large particles. The recent, preliminary air monitoring from the Rodney Street area should be presented and discussed to demonstrate MOE's due diligence on this issue.

Response: Addressed in section 5.6.2 (Part B, Main document) and Appendix 2 (section A2-9.2.1.1).

- 2.5** The statement in the document that the inhalation cancer risks are 10-fold (an order of magnitude) lower than those calculated based upon the Health Canada value should be removed.

Response: Done.

- 2.6** Information on nickel concentrations in ambient air from other locations in Canada/North America will help put the air nickel concentration data from the Rodney Street community into context.

Response: Due to delays in verifying what sort of air sampling equipment was used and the importance of comparing air monitoring data appropriately (discussed in Appendix 2 (section A2-9.2.1.1)), this information was not ready for inclusion in the current draft. This issue is being addressed.

- 2.7** The Panel agreed with the following items, but recommended a more detailed discussion be added to the report for clarification.

- 2.7.1** The air pathway is insignificant in the systemic dose calculation. Nonetheless, this pathway was included in the current assessment.

Response: Addressed in section 4.3.3 (Main document).

- 2.7.2** Because the link between soil levels and ambient air concentrations cannot be reliably estimated, the cancer risk from inhalation exposure was appropriately not used to derive the soil intervention level.

Response: Addressed in section 7-1 (Main document).

3. Market Food Basket and Home Garden Data

Market Food Basket

- 3.1** The Review Panel recommended the use of mean intake values from the Dabeka and McKenzie (1995) data for estimating exposures to nickel from the normal diet.

- 3.1.1** In the Panel's view, upper bound intake values from short-term food consumption surveys may not provide an appropriate estimate of typical long-term food consumption patterns, and the MOE use of a mean value was appropriate.

Response: No action required.

3.1.2 The Dabeka data have been peer-reviewed and published, and represents the author's analysis and conclusions. However, the Panel recognized that the Dabeka data are from one study from the city of Montreal, and may not be fully representative of dietary habits of the Port Colborne population. These uncertainties should be communicated within the uncertainty section of the revised document.

Response: Addressed in section 6.2 (Part B, Main document).

3.1.3 Studies from other jurisdictions (e.g., the U.S. and U.K. market intake surveys) show lower intake of nickel from foods. This provides confidence that the nickel intake from diet would not be underestimated in this assessment.

Response: Addressed in section 6.2 (Part B, Main document).

3.2 The potential reasons for the reported differences between available studies on the Food Basket data on nickel should be discussed in greater detail, particularly the impacts of the use of different cooking utensils and vessels on metal content in foods during preparation/cooking, as well as variation in analytical laboratory methodologies and detection limits. The procedures used to address non-detect nickel concentrations reported in produce need to be investigated and discussed as appropriate in the report.

Response: Addressed in Appendix 4 (section A4-2.3). The treatment of non-detect values has not been addressed in this draft. This issue is being addressed.

3.3 Infant consumption rates for market basket foods should not be based on a proportionate adjustment of adult intake information as conducted by CEPA (1994). The Panel recommended using a more age-appropriate infant diet, as presented by the MOE in the discussion of alternatives within the draft document.

Response: Addressed in Appendix 4 (section A4-2.3). It should be noted that the CEPA infant diet is not derived from adult intake data, but is based on 1970s infant intake survey data.

Home Garden

3.4 The discussion of home grown produce consumption values needs to be expanded and the uncertainty of the various estimates presented. For example, the home-grown produce consumption rate of 9.9% of total produce that was used is higher than those observed in other jurisdictions. These issues should be addressed in the sensitivity analysis, and discussed in the section on strengths and uncertainty of the assessment.

Response: Addressed in section 6.3 (Part B, Main document) and Appendix 6 (section A6-7).

- 3.5** There is insufficient data to support the use of a linear regression to calculate a soil-to-plant uptake factor for nickel. Rather, the Panel recommended that the ministry re-evaluate the available data and select an appropriate upper bound value for plant uptake of nickel.

Response: Addressed in Appendix 3 (section A3-1.4).

- 3.6** There are a number of different fruits listed in the “vegetable” nickel analyses table (page 12 of Appendix 1). The data should be re-evaluated to determine whether fruits, in addition to vegetables, were present in the home gardens found in the Rodney Street community.

Response: Addressed in Appendix 3 (section A3-1.4).

- 3.7** It is likely overly conservative to have potential consumption of home garden produce, in addition to full daily consumption from market basket (i.e., background). The Panel recommends adjusting the market produce consumption rate by the home garden produce consumption, to avoid double counting and exceeding the overall typical daily fruit/vegetable consumption.

Response: Market basket intakes were not adjusted for home grown produce because the use of an upper bound plant tissue nickel concentration from all the aggregated produce types precludes a detailed accounting of the intake of each produce type from either source.

- 3.8** It should be noted in the report that very few of the residences in the Rodney Street area have home gardens. However, the Panel agrees with the inclusion of this pathway so that the assessment may be sufficiently conservative to enable residents to consume home grown garden produce.

Response: Addressed in Appendix 3 (section A3-1.4).

4. Dermal Contact (Contact Dermatitis and Impacts of Oral Intake)

- 4.1** The discussion of nickel-induced contact dermatitis within the assessment report needs to be expanded. The discussion should emphasize that higher levels of exposure are necessary to cause sensitization to nickel than to elicit a response in a sensitized individual. This is a common feature of chemical sensitization in general. However, the available information is inadequate to estimate the magnitude of nickel exposures that could cause sensitization.

Response: Addressed in Appendix 2 (section A2-9.2.4).

- 4.2** The discussion of contact dermatitis should emphasize that contact of sensitized individuals with nickel-contaminated soils has the potential to cause contact dermatitis. The assessment should indicate that the available information does not enable the

identification of a soil nickel concentration that would result in contact dermatitis. Evidence of the low levels of exposure that are needed to cause contact dermatitis from other agents should be summarized to support the conclusion that protection of sensitized individuals by limiting soil nickel concentrations may not be practically achievable.

Response: Addressed in section 7.1 (Part B, Main document).

- 4.3** The Eastside Community Health Study, to be conducted over the next eight to ten months, will be testing people living in the Rodney Street community for nickel contact dermatitis. The results of this study may provide information on the extent and degree of concern on this issue.

Response: Not addressed in this draft. This information is not available yet.

5. Indoor/Outdoor Dust Exposures

- 5.1** The MOE risk assessment treated indoor dust as comparable to outdoor soil. It would be preferable to treat indoor dust as a separate exposure media with distinct characteristics.

Response: In the absence of reliable information on metal concentrations in indoor dust, the contribution of outdoor soil to indoor dust was modeled using literature values (section A6-5.2).

- 5.2** The use of the 10% winter soil cover adjustment to soil ingestion rates and dermal exposures is not considered appropriate for estimating nickel exposure from indoor dust. The Panel recommends removing this adjustment, and include a discussion of the conservatism involved in using the same indoor dust exposure year-round.

Response: Done, discussed in section 6.2 (Part B, Main document).

- 5.3** The relative bioavailability of nickel from outdoor soil and indoor dust required additional discussion. Very little information on this topic is available. One study indicated that bioavailability of dust was slightly higher than that of outdoor soil. This issue requires further discussion in the uncertainty section.

Response: Addressed in section 6.2 (Part B, Main document).

- 5.4** The occurrence of indoor dust reservoirs in inaccessible areas of homes requires additional discussion. Remediation of outdoor soil may not immediately affect indoor dust reservoirs, arising from historical air emissions.

Response: Addressed in section 6.2 (Part B, Main document).

- 5.5** If these indoor dust reservoirs are not disturbed (i.e., extensive renovations), one would not expect indoor dust concentrations to be significantly elevated. Although events such as renovations may result in an elevation of ambient concentrations of nickel of indoor air

and dust, one would expect this to only result in the potential for short-term exposure. As these exposures would only be short-term and are expected to occur infrequently, it would be inappropriate to include in the overall risk assessment.

Response: Addressed in section 6.2 (Part B, Main document).

- 5.6** In the current risk assessment, indoor dust levels were considered to be 39.5% of the outdoor soil level. Available data do indicate that at sites without a significant air source of metals, indoor dust concentrations are generally less than outdoor soil concentrations. However, additional justification should be provided for the value used in the current risk assessment.

Response: Addressed in Appendix 6 (section A6-5.2).

6. Other Metals

- 6.1** The toxicology discussion of cadmium should reference the association between cadmium exposure and osteoporosis. Further information can be found in the following articles:

Järup, L. et al., 1999. Cadmium may be a risk factor for osteoporosis. *Occup Environ Med* 55:435-439.

Staessen, J.A. et al., 1999. Environmental exposure to cadmium, forearm bone density, and risk of fractures: prospective population study. *Lancet* 353.

Response: Addressed in Appendix 6 (section A2-5.2).

- 6.2** The toxicology discussion of antimony should be expanded based upon the new NRC study. The new study is considered more appropriate for exposure from environmental sources. However, antimony was not an issue using the lower exposure criteria. Therefore, the current assessment has an extra margin of safety.

Response: Addressed in Appendix 2 (section A2-2.3.1).

- 6.3** The section on the toxicology of lead should reference the polymorphism of delta-aminolevulinic acid dehydrogenase. Further information can be found in the following articles:

Gerhardsson, L. et al., 1999. Chelated lead in Relation to Lead in Bone and ALAD Genotype. *Environ Res Section A* 80:389-398.

Landrigan, P.J. et al., 2000. The Reproductive Toxicity and Carcinogenicity of Lead: A Critical Review. *Am J Ind Med* 38:231-243.

Response: Addressed in Appendix 2 (section A2-8.1).

7. Bioavailability

- 7.1** While the Panel concluded that the bioavailability adjustments in the assessment were appropriately conducted, the documentation in Appendix 5 requires further clarification of the concept of relative bioavailability in the context of risk assessment.

Response: Done (see Appendix 2 (section A2-1)).

- 7.2** It is recommended that future work on bioavailability should be based on unground soil samples sieved to <250 microns. This approach would ensure that particles so large that they would not adhere to skin, and thus would be unlikely to be ingested, would be removed from the assessment.

Response: Standard MOE SOP is sieving to <350 microns. Changes in our SOP will be considered in future investigations.

8. Uncertainty Discussion

The discussion of the strengths and uncertainties of the Revised 2001 HHRA Study communicates important information to the reader on the degree of confidence in the final soil intervention level for nickel. Therefore, the International Review Panel identified the following issues that could be addressed to improve the overall discussion of uncertainty within the report.

- 8.1** The Panel recommends that the discussion of uncertainty and variability, and the distinction between the two, be clarified. This can be achieved by creating a table that identifies the critical parameters that have uncertainty associated with them, the magnitude/impact of the uncertainty associated with these parameters, and the rationale for the magnitude of the impacts on assessment results.

Response: Addressed in section 6.1 (Main document).

- 8.2** The report should present a table that identifies the critical parameters that have uncertainty associated with them, the magnitude/impact of the uncertainty associated with these parameters, and the rationale for the magnitude of the impacts on assessment results.

Response: A table indicating the impact of changing model parameters as compared with our March 2001 model is included in today's package. This could be the basis for addressing this issue.

- 8.3** A quantitative sensitivity analysis should be conducted to evaluate the relative impact of selected critical parameter on the overall assessment results and conclusions.

Response: See response to 8.2 above.