Port Colborne 2014 CBRA Update Report

Response to MECP Comments

August 28, 2020

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Introduction

In this document, Vale Canada Limited (Vale) provides responses to review comments received from the Ontario Ministry of Environment and Climate Change (currently the Ministry of the Environment, Conservation, and Parks (MECP or "the Ministry")) in a memorandum (dated May 17, 2016) concerning the report entitled 'Port Colborne Community-Based Risk Assessment 2014 Update Report'.

The Ministry has provided several rounds of comments and its dedication to the file is appreciated. There remain some disparities between the Ministry's position and Vale's position on a number of issues, and this response to comments outlines the basis for Vale's position on these issues in 2020, particularly the human health non-cancer TRV (toxicity reference value) for Ni.

The TRV issue is perhaps the single most important issue that has caused Vale and the Ministry to "agree to disagree" about the CBRA HHRA findings, including the large numerical values of the RBSCs (risk-based soil concentrations). Vale believes that the Ministry's "preferred" non-cancer Ni TRV is flawed in several ways and it simply cannot be accepted by Vale, scientifically. Vale has provided detailed analysis of the Ministry's preferred TRV in Annex 2 of this response to comments. That detailed analysis has been provided in the spirit of the Ministry's comment that the CBRA reports must be able to withstand scientific scrutiny. This is true not only for the risk assessment, but reviewer comments, both from the Ministry and others – all must be able to withstand scientific scrutiny. The evidence must be weighed carefully, and a truthful, meaningful assessment should result from these deliberations. Vale believes that this is what has occurred with the Port Colborne CBRA, although there is still some finalization work required.

Throughout this document, the Ministry's comments are presented in Times New Roman font from its original memorandum. Vale's responses to the Ministry's comments are provided in bolded italics, as per these opening remarks, and organized by risk assessment chapter. In many responses, Vale has provided commentary which is intended to provide additional context for scientists and non-scientists alike wishing to understand the risk assessments and scrutinize the weight-of-evidence.

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May 17, 2016

MEMORANDUM

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RE: Review Comments on the Revised Port Colborne Community Based Risk Assessment

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As requested by the Niagara District Office, we have reviewed the most recent submission from Vale Canada Limited (Vale) on the Port Colborne Community Based Risk Assessment (CBRA). This report titled "Port Colborne Community-Based Risk Assessment 2014 Update Report" dated September 12, 2014 was prepared by Stantec Consulting Limited (Stantec) to revise the CBRA to address previous comments provided by the Ministry of the Environment and Climate Change (MOECC or the ministry, and formerly MOE). However, a complete submission was not provided to the ministry for review until March 3, 2015.

Our involvement with this file started in August 2010 when Vale submitted a series of "final" CBRA reports and Addenda Reports on the Human Health Risk Assessment, the Crops Study, and the Ecological Risk Assessment for the Natural Environment. These reports were prepared by Jacques Whitford Limited or Stantec and ranged in date from September 2004 to February 2010 (list of reports provided below). Even though the CBRA started in 2000, the ministry reviewers were intentionally held "in reserve" in order to conduct an independent review. The overall goal of our

review is to ensure that the CBRA has been conducted in accordance with appropriate risk assessment methodologies and practices, that risk has been properly characterized, and that any proposed risk based soil concentrations are appropriate.

We previously provided detailed and comprehensive comments to Vale on the previous CBRA reports in a May 2011 letter to Mrs. Maria Bellantino Perco (Senior Specialist, Environment, Vale) from Camilo Marinez (Coordinator, Community Based Risk Assessment, MOECC). Because of the nature and extent of our comments, and the extensive public review and consultation process that had already occurred, we met with Vale and their consultants on numerous occasions between June 2011 and November 2013 to help Vale understand our comments and resolve outstanding concerns. Our May 2011 comments and responses from Vale are included as part of the CBRA 2014 Update Report (Appendix 1A).

Overall, we reviewed the following Port Colborne CBRA Reports (most of these reports have been included as Appendixes in the CBRA 2014 Update Report but the HHRA Addendum report #1 and the ERA Crops Addendum Report #2 were missing from the update report):

- Port Colborne Community-Based Risk Assessment 2014 Update Report.
- Human Health Risk Assessment "Final Report" dated December 2007.
- HHRA Addendum Report #1 – Response to PLC Consultant Report Human Health Risk Assessment Port Colborne, Ontario dated February 2010. Responds to comments received on Sept 2009 from Watters Environmental Group Inc. (Watters Environmental); the Public Liaison Committee's (PLC) Consultant.
- Crop Studies Report "Final Report" dated December 2004.
- Crops Studies – Addendum Report #1 dated September 2006. Responds to comments received following a public review and comment period on the final Crop Studies Report.
- Crops Studies – Addendum Report #2 dated April 2009. Responds to comments received on Oct 2008 from Watters Environmental.
- ERA Natural Environment "Final Report" dated September 2004.
- ERA-NE – Addendum Report #1 dated March 2005. Responds to comments received following a public review and comment period on the final report and documents the CBRA public review process.
- ERA-NE – Addendum Report #2 dated January 2009. Responds to comments received on Oct 2008 from Watters Environmental.

It addition, we also considered comments on the CBRA reports provided to the ministry on November 2013 by Ms. Diana Wiggins

We recognize that Vale has spent considerable effort to update the CBRA to address our previous comments. However, despite these revisions, the ministry continues to have numerous concerns with the Port Colborne CBRA reports and the proposed Risk-Based Soil Concentrations (RBSC) (also referred to as site-specific threshold levels, SSTLs). Overall, we are unable to endorse the current CBRA or support the proposed RBSC's. Below, we have provided our comments on the CBRA Update report for each chapter. Comments on Vale's responses to our previous comments from May 2011 will be provided in a separate memorandum. In general, we have focused on Nickel (Ni) as the primary contaminant of concern (COC) for our review. Any risk management activities required to address elevated Ni contamination in soil are anticipated to also address the other metals of concern (i.e., Arsenic, Copper and Cobalt).

Vale response: The Port Colborne Community-Based Risk Assessment (CBRA) process has been underway since year 2000, with several years of prior preparatory discussions between Inco and the Ministry. From the outset, the goal of the CBRA was to evaluate the potential human health

and environmental risks associated with the metals in soil that are attributed to the historical emissions from Inco's Port Colborne Nickel Refinery, for which the company has accepted responsibility. The 2014 Update Report was intended to be a consolidation of the individual risk assessments (Human Health, Ecological – Natural Environment, and Ecological – Agricultural Crops) which would serve as the primary source of information concerning the potential risks associated with the chemicals of concern (CoCs) identified within the CBRA process (nickel, copper, cobalt and arsenic).

Vale Canada Limited believes that the risks have generally been characterized appropriately, although it must be acknowledged that there are some aspects in which the CBRA risk assessment reports never did, and still do not represent standard practice. Vale is proposing further follow-up activities in the Port Colborne Community-Based Action Plan (PCCAP) with the intention of addressing outstanding Ministry concerns to the extent possible.

Comments on Chapter 1 – Introduction

1. **Section 1.0.** This section provides background information on the overall CBRA, various challenges in conducting the assessment, and subsequent discussions that were held to address ministry review comments from May 2011. To be clear, the fact that independent ministry reviewers were involved in the technical review is not a limitation of the review process and should not be seen as the reason for the extensive concerns that the ministry raised. The final CBRA report should be able to withstand scientific scrutiny from anyone qualified to review risk assessments; not just those involved in conducting the CBRA.

Vale Response: This introductory section provided context for the reader. Surrounding the Ministry's comments provided to Vale in 2011, there was considerable discussion and development of the understanding on Vale's part that the Ministry's reviewers did find it difficult to review the CBRA component risk assessments. The extensive concerns show good engagement from Vale's environmental regulator and are appreciated. Scientific scrutiny is, of course, critical to achieving a successful, truthful risk assessment.

2. **Section 1.1, page 1.7.** The 2nd paragraph should indicate that in addition to the additional soil investigation, the MOE 2002 report also contains the results of the Human Health Risk Assessment that was conducted by the ministry for the Rodney Street Community. A brief summary of the Rodney Street HHRA could also be added at the end of Section 1.2.1.

Vale Response: Comment received. Vale does not intend to re-engage the consultant to revise the reports, so it will be known to interested parties only via this comment-response dialogue that the Ministry has provided this comment. The Ministry's Rodney Street Risk Assessment report was referenced several times and cited in Chapter 2 (Site Characterization) as well as in Chapter 3 (Human Health Risk Assessment).

3. **Section 1.3.3.** While the two large farms were not sampled as part of the CBRA, the risk based soil concentrations developed from the crops study should still apply to them; hence they are not excluded from the CBRA.

Vale Response: Comment received. While not sampled, the farms were certainly in the zone of impact from historical refinery emissions. The findings of the CBRA are applicable to these properties. The owners may require additional sampling to determine how the CBRA findings would be relevant for the properties.

4. **Section 1.6.** The CBRA does not provide any information on ecological risks for "human-influenced environments such as parks, playgrounds, gardens, and residential yards". Given the absence of a formal risk assessment for these areas, information from the ERA natural environment and the crops study should be used to establish appropriate risk based soil concentrations for these areas to allow for reasonable use that is not impacted by elevated COCs in soil.

Vale Response: The human-influenced environment was excluded from the CBRA process, as agreed by the TSC (Technical Subcommittee) at the time. The Update Report included the consideration of an additional receptor, the red fox, as a surrogate for a pet such as a dog living in the human-influenced

environment. It is understood that the Ministry considers the use of the **Modified Ecological Protection (MEP)** ***approach inappropriate, and Vale accepts this concern. As such, new risk calculations are provided below (see Annex 1) to demonstrate that under a worst-case exposure scenario, using concentrations of CoCs identified in Woodlot #17 (the "Reuter Road" woodlot), and the adjacent field environment. The results indicate that unacceptable risks would be anticipated for a family pet (using the red fox as a surrogate for a pet dog) exposed to the extreme concentrations identified in Woodlot #17. However, in the adjacent field environment (soil Ni concentration of 3,147 mg Ni/kg soil and Ni concentrations in food items of 5.48 mg/kg fresh weight), the risks would be calculated to be acceptable.***

Regarding risk to non-agricultural plants, unacceptable risks to populations of certain plant species could be calculated for both the field and woodlot, based on information contained within the Crops Risk Assessment, as proposed by the Ministry. Vale has continued to promote analysis and publication of the previously collected data from the CBRA. An example of Vale's continued interest in the effects of legacy metal deposition on terrestrial ecological communities, including that of the human-influenced environment, please refer to Hale and Robertson (2016 [Env. Poll.212: 41-47]) in which measures of woodlot health have been linked to soil metal concentrations in the Port Colborne region. That paper was derived from the woodlot studies conducted as part of the CBRA.

5. **Section 1.8.** The CBRA reports and addenda reports were not formally reviewed by the ministry until August 2010.

Vale Response: Comment received.

6. **Section 1.9.** The HHRA Addendum Report #1 should be included in this section (Response to PLC Consultant Report, Human Health Risk Assessment Port Colborne, Ontario dated February 2010).

Vale Response: Comment received. The PLC's consultant was delinquent in providing their review comments, which were not received until January 2011, several months after the PLC had produced its final report. The document referred-to in the Ministry's comment is entitled, "Response to PLC Consultant Report Human Health Risk Assessment Port Colborne, Ontario", marked draft, and is dated February 23, 2011.

Comments on Chapter 2 – Site Characterization

7. **Section 2.5, page 2-12.** While excluded from the CBRA, these industrial lands (i.e., the refinery property) should be identified in future risk management plans as a potential source of COCs to the surrounding area if the soil is disturbed. Measures to minimize this pathway may already be in place and should be summarized in the planned Implementation Report.

Vale Response: The Refinery site has a Closure Plan, most recently submitted to the Ministry of Energy, Northern Development and Mines in May 2019. The closure plan is a legal requirement under the

Mining Act, and given the planned closure date of 2042, and risk management related to lands covered by the CBRA must, as a practical matter, be kept separate, but certainly Vale is aware that risk assessment will be a valuable tool to guide closure planning.

8. **Section 2.6., page 2.12.** Presumably, this section is referring to Table 2-2 since there is no Table 2-4 in Appendix 2A. The focus of these comparisons is to show that Ni levels are much higher in woodlot soils than in nearby field soils. That is not in dispute. However, given the extensive data collection summarized in Section 2.1, it is surprising that only 3 comparisons are made and that two of the locations are over 4 km away from the refinery (e.g., only one comparison occurs within the original primary study area).

Vale Response: Error in table numbering noted. It should have been Table 2-2 as noted by the Ministry's comment. The table was not meant to be exhaustive, but illustrative of the fact that woodlot canopies concentrate metal particulates relative to adjacent but leeward field environments, an important aspect of site characterization. The fact that only three examples were used in this table does not materially affect the findings of the CBRA. In fact, the site just a km from the refinery was the most extreme illustration of this phenomenon. Table 2.2 should be read in conjunction with section 2.6.

9. **Section 2.8.3.** This section should note that while fish may not be present, these intermittent drains and ditches still provide habitat for aquatic organisms when water is present and that organisms may be exposed to elevated COCs from water and sediment. This is one of the reasons that amphibians were evaluated in the risk assessment. Also, information should be provided on the sediment and surface water samples collected and summarized in Table B-3 (Primary and Secondary Study Areas, and Control Area Sediment Concentrations Used in Revised Risk Calculations) and Table B-4 (Primary, Secondary, and Control Area Surface Water Concentrations Used in Revised Risk Calculations).

Vale Response: See response to comments 15 and 19 below under the section Specific Comments on "ERA-NE Report" and Annex 1.

Comments on Chapter 3 – Human Health Risk Assessment

The following provides a brief summary of the ministry's review of the Human Health Risk Assessment component of the Port Colborne CBRA Updated Report 2014. As soil Ni is the most significantly elevated COC in the community above background levels and human health based soil criteria, the review focuses on the toxicity, and potential exposure to Ni. This review considers the information within the revised CBRA report, as well as additional information from other regulatory agencies and current scientific literature, in order to better characterize the risks from Ni exposure and identify appropriate Ni Risk Based Soil Concentrations (RBSCs). RBSCs were developed for the toddler receptor as they have higher contact rates with soil and are still developing into adults.

Overall, the ministry has numerous major concerns with the revised CBRA that are provided in detailed Appendixes at the end of this memorandum. These concerns include:

- The oral Ni Toxicity Reference Value (TRV) that was used as the toxicity benchmark
- How dietary background exposure was estimated

- The bioavailability and bioaccessibility of Ni in soil
- How outdoor soil was used to estimate indoor dust concentrations
- The Ni soil ingestion rate that was used to estimate exposure to the Toddler

As these concerns are significant in nature and have not been resolved, specific comments on Chapter 3 are not provided.

Vale Response: In the HHRA, Vale believes that the Ni TRV selected to characterize human health risks and establish corresponding risk-based soil concentrations (RBSCs) in Port Colborne represents the most significant divergence of opinion between Vale and the Ministry.

Three of the issues in the bulleted list above (i.e., dietary background exposure estimates, the methods used to approximate indoor dust concentrations, and the soil ingestion rate among toddlers) are a matter of professional/scientific judgment. Vale accepts the Ministry's selected approaches and suggested numerical values to be used in the CBRA HHRA for these three aspects of exposure estimation as they are within a range of reasonable values. However, Vale strongly disagrees with the Ministry in the areas of (1) Ni TRV selection, and in particular, the underlying science selected by the Ministry from other jurisdictions around the world, and (2) the bioavailability and bioaccessibility of Ni in soil (and food). This will be discussed below in detail in Annexes 2 and 3.

Overall Conclusions on the Oral Ni TRV (Appendix A): The ministry does not support the Ni TRV used in the revised CBRA for assessing oral Ni exposure. A TRV is the benchmark used in risk assessment as an indicator of the maximum acceptable daily dose to which a person may be exposed without adverse effects. The oral Ni TRV of 20 micrograms per kilogram body weight per day (µg/kg-bw/day) used in the CBRA is based on adverse changes in body weight and organ weight observed in exposed test animals (rodents). This TRV was originally supported by the MOECC as noted in previous ministry comments (MOE 2011). However, based on the most up- to-date scientific information, changes in weight are no longer the most sensitive endpoint to use in assessing oral Ni exposure. Instead, the MOECC supports a TRV of 11 µg/kg-bw/day based on adverse reproductive and developmental effects observed in rodents.

Overall, the TRV of 11 µg/kg-bw/day is considered by the MOECC to be appropriate for the protection of Ni-associated reproductive and developmental adverse effects, including the potential toxicity of Ni in developing male reproductive organs. However, it must be noted that this TRV may not be fully protective of Ni-sensitized individuals from the development of dermatitis. Finally, this TRV of 11 µg/kg-bw/day is supported by Health Canada (2010), the

World Health Organization (WHO, 2007) and the Office of the Environmental Health Hazard Assessment, California Environmental Protection Agency (OEHHA, 2012) and the analysis by the European Food and Safety Authority (EFSA , 2015). This TRV represents the most up-to-date value to use in risk assessment as an indicator of the maximum acceptable daily dose to which a person may be exposed without adverse effects.

Vale Response: There is considerable new information regarding TRVs since the 2014 Update report was submitted to the Ministry. Since then, the European Food Safety Authority (EFSA) has conducted a draft re-assessment of the oral Ni TDI (tolerable daily intake – a type of TRV) (https://www.efsa.europa.eu/en/topics/topic/metals-contaminants-food). This latest TDI replaces the EFSA (2015) value referenced in the Ministry's comment, which has since been shown to be an

erroneous value.

In 2019, the Human Toxicology and Air Standards (HTAS) Section, Technical Assessment and Standards Development Branch (TASDB) of the Ministry released an approved oral TRV for Ni of 11 µg/kg/d, as per the document entitled: 'Human Health Toxicity Reference Value (TRVs) Selected for Use at Contaminated Site in Ontario' (MECP, 2020). The Ministry's rationale for the selection of this TRV was summarized in a 2019 document entitled 'Toxicity Reference Value (TRV) Selections for Nickel (Ni) various CAS#' (MECP,2019). Effectively, the rationale used by the Ministry for the selection of an oral Ni TRV (of 11 µg/kg/d) was the adoption of a TRV derived by California Environmental Protection Agency (OEHHA, 2001, 2005). In earlier discussion with Vale prior to the 2014 Update Report, the Ministry had used TRVs derived by the DEPA (2008), the OEHHA (2012), HC (2010), and the European Food Safety Authority (EFSA, 2015) as justification for TRV 11.

Vale rejects the validity of the 11 µg/kg/day TRV ("TRV 11"), the reasons for which are explained in more detail below in the comment-response dialogue and in Annex 2. The acceptance of the TRV 11 by the various agencies listed above (OEHHA, Health Canada, etc.) requires scientific scrutiny and should not be accepted as correct without detailed analysis. The rationale presented in MECP (2019) for the selection of "TRV 11" does not suggest the Ministry performed detailed scrutiny of the underlying scientific information, but rather, suggests acceptance, at face value, of analyses conducted by other regulatory agencies. Regulatory Agencies (competent authorities) are not infallible, and the citation chain provided by the Ministry above should undergo scientific scrutiny, which Vale has provided in Annex 2 below in response to the specific comments provided by the Ministry on this particular issue.

Overall Conclusions on Dietary Exposure (Appendix B): The ministry does not support using the estimated Ni concentrations in garden produce and supermarket foods that were developed for evaluating dietary Ni exposure in this CBRA, despite the extensive work that was done by Vale in attempting to develop a Port Colborne specific estimate for this exposure pathway. Deficiencies in sampling of both garden produce and supermarket food significantly limit the interpretation of these results and the final CBRA estimates for the Port Colborne diet fall within the low range of the expected community exposure of Ni through the diet. Instead of the estimates proposed in this CBRA, the ministry recommends that the overall average estimate from Health Canada's Total Diet Survey's between 2000 and 2007 should be used instead. Supermarket exposure should be similar throughout Canada and given that the available data from the CBRA update report clearly indicate that Ni is elevated in local garden produce (i.e., locally grown fruits and vegetables), dietary exposure to residents of Port Colborne should be higher than the Canadian average; not lower as indicated in the report.

Vale Response: The garden and supermarket food surveys were conducted by Inco's consultants with the guidance of the TSC (Technical Subcommittee) and the PLC's (Public Liaison Committee) consultant. There were necessarily sampling limitations in the Port-Colborne-specific analyses. As a result of discussions held between Vale, its consultant, and the Ministry between 2011 and 2013, a revised approach to dietary intake was adopted in the 2014 Update Report. Vale believes that the inclusion of locally obtained supermarket produce metal data (with regional/national data as well) is preferable to data collected from distant Canadian locations for which the food supply source is likely from different jurisdictions.

Regarding backyard fruits and vegetables, the 90th percentile values from the entire Port Colborne garden dataset were used in the Update Report. These data are provided in Appendix 3B of the Update Report. There is no national database containing metal concentrations in backyard garden produce. Local data are essential to developing the best possible exposure estimates for Port Colborne residents.

Overall Conclusions on Bioaccessibility (Appendix C): The ministry supports the general argument that not all of the Ni in soil is biologically available. That is, if a person consumes soil containing Ni, not all the Ni would be available for absorption from the soil in the gastrointestinal tract (i.e., bioaccessible) and the resulting absorption of Ni into the bloodstream would be less than 100% (i.e., bioavailable). However, the ministry does not support the approach used in the risk assessment to estimate the bioaccessibility of Ni. Specifically, the ministry believes that the estimates are too low and, for the purpose of this risk assessment, underestimate Ni exposure from soil and the risk resulting from incidental ingestion.

Vale Response: Vale disagrees with the Ministry on this matter, but recognizes that the Ministry's approach would lead to a conservative assessment of human health risk. However, the comment indicating that the Ministry "…believes that the estimates are too low and…underestimate Ni exposure from soil…." requires supporting scientific justification. Further detailed discussion follows in Annex 3 below in response to the specific comments provided by the Ministry.

Overall Conclusions on the Outdoor Soil to Indoor Dust Ratio (Appendix D): Based on a limited number of samples, the ratio between Ni in indoor dust and Ni in soil was estimated in this CBRA to be 0.2 (i.e., dust contains 20% of the total Ni that is found in soil from the Port Colborne community). This ratio was used in the CBRA to estimate the Ni concentration of indoor dust from measured Ni concentrations in soil as part of developing the RBSC. The ministry has concerns with this ratio primarily because the dataset is too small to develop a robust estimate and also because the ratio of Ni in indoor dust to Ni in soil is often much higher than 0.2 when soil Ni concentration is less than 2,000 mg/kg.

Vale Response: Vale recognizes that the Ministry's approach would lead to a conservative assessment of human health risk. Further discussion follows below in the comment-response dialogue in response to the specific comments provided by the Ministry.

Overall Conclusions on Soil Ingestion Rate (Appendix E): The ministry has considered the alternative incidental soil ingestion rate (SIR) of 110 mg/day for the toddler receptor and finds that it is reasonable for use in the CBRA. However, this represents a Central Tendency Exposure (CTE) estimate in the calculation of exposure from the soil and dust pathways. The ministry also considers the SIR of 200 mg/day to be valid for use in the CBRA as a Reasonable Maximum Exposure (RME) estimate. The SIR of 200 mg/day has been identified as a conservative assumption (MOE, 2011) and MOECC maintains its use in the development of Brownfields (O. Reg. 153/04) soil standard setting. The incidental SIR is the key exposure assumption used in the CBRA in estimating exposure from the combined soil and dust pathways. As the SIR does not distinguish between soil and dust it may be assumed for both the soil and dust exposure pathways by using the 45:55 ratio as assumed in the US EPA's Integrated Exposure and Uptake Biokinetic (IEUBK) model for lead in children (US EPA, 2002). In addition, as done in the CBRA, the soil pathway may also be pro-rated for winter snow cover, where exposure to soil outdoors is considered negligible or zero.

Vale Response: Vale recognizes that the Ministry's approach would lead to a conservative assessment

of human health risk. Further discussion follows below in response to the specific comments provided by the Ministry.

Overall, based on our review, the ministry has determined that the most appropriate oral TRV for Ni is 11 µg/kg-bw/day. This TRV is based on both reproductive and developmental effects observed in animals. However, background dietary exposure to Ni makes up the majority of the exposure to the toddler and is also estimated to be 11 µg/kg-bw/day. Thus, background dietary exposure to Ni – irrespective of any elevated soil Ni exposure for conditions in Port Colborne – is similar to the health based toxicity benchmark. Given this fact, an alternative approach will need to be considered that allocates an appropriate amount of overall Ni exposure to soil. Because of these concerns, the ministry believes that the revised CBRA currently underestimates the potential risk from Ni exposure in Port Colborne soils to toddlers in some areas of Port Colborne with elevated Ni levels in soil.

Vale Response: Vale strongly disagrees with the Ministry's assessment. TRV 11 is scientifically unsound for reasons discussed below in the response to specific TRV comments (i.e., in the Ministry's Appendix A) and Annex 2 of this Response to Comments.

Comments on Chapter 4 – Natural Environment Environmental Risk Assessment

Based on comments the ministry provided in May 2011, Stantec has substantially revised the format and approach of this ecological risk assessment for the natural environment. Instead of estimating risks based on averaging soil concentrations across the entire study area, the revised approach now focuses on the most contaminated lands that are closest and downwind of the refinery to determine potential risks to ecological receptors. However, the revised approach incorrectly uses the Modified Ecological Protection (MEP) option under O. Reg. 153/04 to characterize the risk for the entire Port Colborne natural environment (i.e., non-residential woodlots and non-agricultural fields). This MEP option is specific for individual properties being evaluated under O. Reg. 153/04 if certain conditions are met and requires a certificate of property use to inform future land owners that adverse effects may occur to some plants, soil organisms, and wildlife that might reside in or frequent the site. The MEP approach is not appropriate for identifying and characterizing risks for large scale ecological risk assessments as it uses less stringent eco-toxicity values to develop site-specific soil standards. No information is provided on potential risks without the MEP option. Additional site characterization information has been provided which addresses many of our previous comments relating to site characterization. In addition, the ERA now includes some new water surface water quality data for the Wignell and Beaverdams drains for use in further characterizing risks to amphibians. However, there remain significant concerns with this risk assessment and the ministry is not in a position to accept the proposed site-specific soil intervention values as appropriate for the Port Colborne natural environment.

Vale Response: The use of the MEP approach may be controversial, but the following passage is taken from the Ministry's guidance regarding MEP in the Nov., 2016 document on the Modified Generic Risk Assessments under the Brownfields Regulation:

In order to allow the development and application of less stringent PSS, current practice in Ontario may be to remove ecological habitat to ensure no ecological species are present or exposed to contamination. This practice results in the removal of habitat which, although degraded, could and often does support a variety of ecological species. While redevelopment needs may drive the removal

of habitat, the ministry's intent is to provide another option that will allow for greater preservation of ecological habitat. The ministry has developed a "modified ecological protection (MEP)" option within the Approved Model, which is intended to both promote brownfield redevelopment and preserve existing and potential future ecological habitat. This means getting more brownfield properties developed and providing developers a greener alternative to paving over ecological habitat. The ministry will continue to look at new ways of promoting ecological habitat preservation as part of brownfield redevelopment.

> ***MEP is an option available to risk assessors within the MGRA process in Ontario that uses less stringent ecotoxicity values to develop PSS. The use of the MEP option will allow for the maintenance or establishment of natural habitat; habitat that is not comparable in quality to habitat in an uncontaminated setting, but instead is habitat comprising of assemblages of species that are adapted or less sensitive to the contaminants of concern at the property. Use of the MEP option may result in impacts to some plants, soil organisms and wildlife that might reside in or frequent the site. The MEP option does provide the same degree of protection to humans as the Tier 1 generic standards.***

While it is true that the Brownfields Regulation is intended to be used at specific properties and not for wider area contamination as seen in Port Colborne, there are certainly parallels between the situation in the natural environment at Port Colborne and those at individual properties anywhere in Ontario having contaminated soil issues. The reality is that there is dispersed Ni, Cu, Co, and As contamination due to legacy operation of Inco's Ni refinery. The ecosystems appear to be functioning more or less normally, and a citizen walking through the Reuter Road Woodlot (Woodlot #17) would likely not notice anything different from any other woodlot they have walked through in their lifetime, even though experts familiar with the woodlot would be able to say that soil invertebrate communities and soil decomposer communities are impaired, associated with soil Ni concentrations ranging from 10,000-33,000 ppm.

How to manage these contaminated natural areas remains an open question. Vale is moving forward to study options for these natural areas, of which there are a small number immediately to the east of the Refinery property. Natural forces (Climate change, development, invasive species) are likely contributing to the structure of these woodlots, common to woodlots across the southern range of the province. It is possible that, as envisioned in the Integration Report previously released by Vale, these woodlots should be left to naturally recover. The MEP approach provides a different lens for viewing these risks within that context. Vale recognizes that non-MEP risk calculations should be undertaken, and several "worse-case" (sic) (i.e., worst-case) scenarios are provided in this comment-response dialogue for clarity. See Annex 1 for details.

Specific Comments on ERA-NE Report

10. **Page 4-2. Ecological Risk Assessment Objectives and Scope.** As noted, the "ERA focused on the natural environment: human-influenced environments such as parks, playgrounds, gardens, and residential yards were not considered". However, these human-influence environments are not addressed elsewhere in the various CBRA reports and represent a limitation in the CBRA report that will need to be addressed. While this may have been an acceptable approach when the CBRA was started, it is no longer the case that

these human-influenced environments can be overlooked. However, information is available from the Crops ERA and this ERA-NE to develop appropriate soil thresholds for the protection of soil invertebrates, residential gardens, and grasses, shrubs, and trees that would be expected in these environments.

Vale Response: The CBRA process did not consider these human-influenced environments specifically. (See comment-response for comment #4 regarding the Introduction of the 2014 Update Report, above.)

11. **Page 4-4, Section 4.2.2.1. Site Description.** As noted in previous ministry comments, some woodlots have too few samples to properly characterize the variability in the patchiness of COC concentrations. As a result, additional data collection may be needed for some woodlots to determine if they have acceptable COC concentrations or not.

Vale Response: Vale will not support further data collection under the CBRA process. Vale believes that the worst-case risk scenarios addressed for the Reuter Road woodlot (Woodlot #17) in the original CBRA NE ERA) and adjacent fields (see Annex 1) along with the Update Report and the original Natural Environment ERA, provides sufficient context that would allow risk management plans to be developed for these, the most contaminated woodlots. Further sampling analysis of Woodlot #17 is planned, but this would take place outside of the CBRA process.

12. **Page 4-5, Section 4.2.2.3 Data Used in the ERA.** This section should include the detailed maps illustrating sample location by receptor and environmental media that were provided separately as hardcopy to the ministry.

Vale Response: The Ministry is referring to figures which are now provided in Annex 4 of this response to comments. The figures can't be added to the Update report directly, as the Update Report is considered to be a final report.

13. **Page 4-6. 1st paragraph.** In general, the MOECC agrees with the approach of using the 95% UCLM as a reasonable worse-case woodlot and adjacent field scenario (although, see comments #17 and 18 below). However, using the 95% UCLM will not result in an overly conservative prediction of potential exposure and subsequent risk as noted in the report. Instead, the risk-based estimate for this woodlot and nearby field area will be appropriate for predicting potential impacts across the entire site as they can be adjusted to determine the risk threshold where soil concentrations are equal to a HQ of 1.0. Also, there was not a "perceived influence of unequal distribution of sampling"; this was a fact as described in previous Ministry comments.

Vale Response: This passage was poorly worded. The issue discussed was that the UCLM is sample-size dependent. When fewer samples are present in a data set, the UCLM could be larger than the highest value in the dataset. The statement mentioning unequal distribution of sampling simply refers to that phenomenon.

14. **Page 4-7.** Table 4-1 shows a very limited dataset and only includes 1 example of data close to the refinery; the other 2 are over 4km away. Using the data provided in Tables B1 and B2, the average COC concentrations from the worse-case scenario woodlot and field scenario are likely a better example for conditions close to the refinery (e.g., mean

Ni in woodlot = 18,000 mg/kg; mean Ni in nearby fields = 1,870 mg/kg). Similarly, using data from the woodlot 1 km to the East of this area provides a better example of the decrease in COC levels (e.g., using woodlot data from LL19, SSH1 to SSH3 and field data from CSH7, CSH8, OSH27 and OSH28 results in average Ni concentrations of 2,700 mg/kg in woodlots and 930 mg/kg in nearby fields). It is also important to note that the difference in COC concentrations between the woodlots and the fields are less at woodlots and fields farther away from the refinery.

Vale Response: It is true that Table 4-1 is based on a limited data set. Vale agrees that the difference in CoC concentrations in woodlots and adjacent fields diminishes with distance. With distance, there was less metal load in the air to be concentrated in the windward portions of the canopies of the woodlots and (because of this fact) less difference between woodlot soils and those in the adjacent fields with increasing distance from the refinery. Fortunately, for the purposes of this discussion, the most-contaminated woodlot highlighted in Table 4-1 represents the worst-case scenario for evaluating risk.

15. **Page 4-8.** Even though the aquatic features are intermittent in nature (ponding in woodland swamps; ephemeral conditions in Wignell and Beaverdams drains), aquatic receptors may be exposed to elevated COCs when these features are present and risks associated with this exposure should be characterized.

Vale Response: This comment is discussed below at comment 19.

16. **Page 4.11. Section 4.2.3.2. Identification of Receptors.** Table 4.2. No major concerns with using MOECC VECs from the generic model in the revised risk assessment except for evaluating plants, soil invertebrates and decomposers. These receptors should continue to be assessed separately and not as a group (especially since site-specific data is available from the Crops ERA (e.g., for herbaceous plants) and the Natural Environment ERA (e.g., site-specific information for maple trees, soil invertebrates and decomposers).

Vale Response: Comment received.

17. **Page 4.13, Section 4.2 4.1. Exposure Point Concentration.** The revised CBRA uses the 95% UCLM as the exposure point concentration based on the rationale that this upper estimate of the central tendency is appropriate for evaluating the "population" of non- mobile soil invertebrates and plants. However, we recognize that exposure will exceed these values in some places and that risks will be higher for organisms exposed to concentrations above the 95% UCLM. Areas in excess of the 95% UCLM should be identified and if discrete contiguous areas in excess of the 95% UCLM are present (e.g., contaminated hot spots), then it may be necessary to evaluate risks at the maximum concentration for those areas as well. Overall, the areas potentially impacted by elevated COC concentrations in soils needs to be clearly delineated.

Vale Response: The "Safe" Soil CoC concentration, as determined in the Update Report is well below the UCLM. See Table 4-16 in Update Report. For consideration, risks in "hot spots" are represented by the maximum value of 33,000 ppm Ni (see Annex 1). Further delineation would be valuable for risk management. Delineation of the Ni contamination will be undertaken in PCCAP follow-up activities.

18. **Page 4.13. Table 4-5.** No concern that the 95% UCLM for woodlot #3 is an appropriate upper estimate of central tendency exposure that would be expected in any woodlot in the Port Colborne area. However, some concerns with the corresponding "worse-case" field scenario as

several relevant soil samples are not considered (e.g., data from IH2 and IH4 are not used yet they have elevated Ni concentrations of 3,790 and 2,600 mg/kg respectively). Hence, the 95% UCLM may be too low to characterize the field habitat.

Vale Response: See Annex 1 for the detailed response to this comment.

19. **Page 4.14.** BLM modelling has been conducted on a very limited dataset (n=3 for Beaverdams; n=6 for Wignell) from water samples collected from only one sampling event on Oct 3, 2013. No rationale is provided on if parameter values (e.g., for pH, DOC and hardness) would be expected to vary over the course of the year and if modelling water quality conditions in October are appropriate. In addition, total concentrations of COCs collected in 2013 from these drains are much lower than the concentrations measured from the intermittent ponds and used in the risk modelling of other receptors (see Table B-4). For example, the EPC for Ni from the primary areas is 1,063 ug/L whereas the EPC for Ni from the Wignell drain is 8.3 ug/L (reduced to a BLM EPC of
3.5 ug/L) and the EPC for Ni from the Beaverdams drain is 19 ug/L (reduced to a BLM EPC of 1.4 ug/L). In fact, except for Co, the maximum concentrations are less than the applicable PWQO (max Cu = 1.9 ug/L; max Ni = 19 ug/L), hence, there would be no need to model bioavailability as total concentrations in these drains on this date were acceptable.

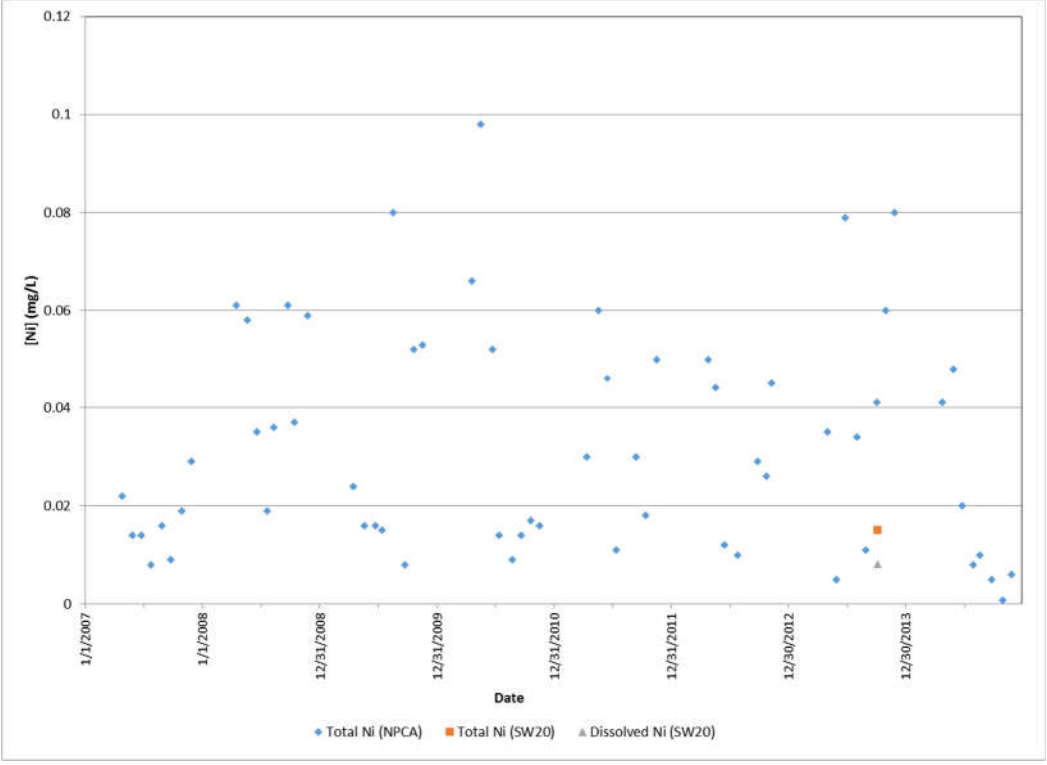
Vale Response: The PWQO can now be considered to be an outdated dataset. The BLM represents the most current scientific approach to assessing risk in freshwater environments, with the European Union having developed a BLM-based water quality standard for Ni in freshwater of 4 µg/L (as bioavailable Ni). In late 2016, the OECD published a Guidance Document under the auspices of its Testing and Assessment program (Publication No. 259) entitled, "Guidance on the Incorporation of Bioavailability Concepts for Assessing the Chemical Ecological Risk and/or Environmental Threshold Values of Metals and Inorganic Metal Compounds". The document is available at http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)66&doclanguage=en ***. This document represents the "latest science" on this topic.***

The consideration of bioavailable Ni, Cu, and Co concentrations in a limited sample set was intended to provide further knowledge on the matter, given that the CBRA has spanned 20 years, beginning at a time when BLMs had not yet been conceptualized. The current best and most scientifically sound approach for assessing aquatic risk is via the use of BLMs, which correctly evaluates the risk due to dissolved metal ions and also considers water hardness, pH, and dissolved organic carbon. Toxicity and risk are a function of all four of these factors. The reassessment of aquatic risk in the Update Report used the most up-to-date scientific approach to assess the off-site aquatic risk.

It should be noted that three of the water samples included in the 2004 Natural Environment Risk Assessment and in the 2014 Update Report (samples S1, S2, and S3 containing 101, 884, and 626 µg Ni /L) were considered to be in the primary study area. In fact, these were all from the active Port Colborne Refinery Site and as such, should be excluded from consideration in the CBRA (because the refinery site is still an active operation under the Mining Act and has its own closure plan). When these samples are excluded, the remaining water samples were all less than 29 µg Ni /L in unfiltered water samples, which is similar to the values measured in the Wignell and Beaverdam Drains in 2013

and assessed via BLM. The following figure provides further context.

Total aqueous Ni concentrations in the Wignell Drain, slightly upstream of the control structure near the Lake Erie shoreline were obtained from the Niagara Peninsula Conservation Authority (NPCA). The NPCA periodically produces Water Quality Monitoring Reports, and the 2016 report is available at https://npca.ca/water-quality. The figure below shows total Ni concentrations from the Wignell Drain from 2007-2014. In addition, the total and dissolved Ni concentrations from the October, 2013 sampling event are included.



These NPCA data and Vale's 2013 sampling and subsequent use of the BLM do corroborate the Ministry's comment that the aquatic risks have not been adequately characterized by today's standard. There are many questions that should be asked about aquatic risk. Are the elevated aquatic Ni concentrations seen in the figure above related to runoff of soil particles from the impacted lands associated with rain events? Do they contribute to toxicity, or do the total metal concentrations reflect the presence of poorly bioavailable Ni associated with suspended particulate matter? Is there any metal-associated toxicity? What about agricultural impacts? The NPCA data show that phosphate, suspended solids, and E. coli concentrations are elevated in the Wignell Drain, which is also known to impact Gravelly Bay. What about risk due to pesticide run-off from agricultural and commercial use? What about the contribution to risk from upstream industrial activities (quarry dewatering and industrial effluent releases)? How are these risks to be assessed in addition to those of the CoCs from the Port Colborne Refinery legacy operations? Vale recognizes that the aquatic risks in the original CBRA Natural Environment Risk Assessment are not characterized by today's standards,

the original CBRA data collection and analysis occurred two decades ago. The assessment of risk in these drains will be updated via follow-up activities under the PCCAP.

20. **Page 4.15.** No information is provided for the EPC for sediment. Table B-3 provides data but it is not clear if it is used in the risk assessment.

Vale Response: Sediment risks were not calculated in the Update Report. As mentioned in the response to the previous comment, there is likely to be considerable confounding due to agricultural and current industrial uses in the Wignell Drain watershed. Also, as these are municipal drains, they are periodically dredged of sediment, as the majority of the Port Colborne Drain was in 2016. Sediment risk will be evaluated under the PCCAP.

21. **Page 4.15. Section 4.2.4.2. Calculation of Tissue Residues for Food and Forage.** No information has been provided on what site-specific uptake factors were used in this assessment and if they are appropriate to use at the soil Ni concentrations found under the "worse-case scenarios" tested. The update report simply cites the previous 2004 risk assessment. A comparison between the site-specific uptake factors used in this risk assessment and the generic BAFs provided in the generic model (MOE 2011) should also be provided. As an example, the reviewer was unable to duplicate the estimated Ni uptake into terrestrial plants provided in Table 4.7.

Vale Response: Vale also could not duplicate the estimated Ni uptake in Table 4.7. Revised example calculations are provided below in Annex 1.

22. **Page 4.16 Section 4.2.4.3. Calculation of Average Daily Dose for Birds and Mammals.** No information has been provided on what site-specific absorption factors were used in this assessment and if they are appropriate to use at the soil Ni concentrations found under the "worse-case scenarios" tested for the receptor evaluated.
The report refers to information in Appendix 3.E of Chapter 3 of this update report but no specific information is provided here. For consistency, a comparison between the site- specific absorption factors used in this risk assessment and the factors provided in the generic model (MOE 2011) should also be provided.

Vale Response: Comment received. Revised example calculations are provided below in Annex 1.

23. **Table 4.8 and 4.9.** It is difficult to determine how the total average daily dose (ADD) was calculated for mammals and birds in the woodlots and adjacent field. The information provided in Appendix C is difficult to review and insufficient as no rationale is provided for any of the inputs. Additional rationale is needed to support why the ADD for some receptors in the woodlot are so low when compared to the adjacent field given the much higher soil EPC for the woodlot. For example, the estimated total ADD for the short-tailed shrew (90 vs 165 mg/kg-day) and woodcock (98 versus 207 mg/kg-day) are all lower in the woodlot than the adjacent field even though Ni concentrations are 10 times higher in the woodlot.

Vale Response: There certainly appears to be a calculation error that the Ministry has uncovered. Also, Vale agrees that the consultant's proprietary ecoRAM printout model provided in Appendix C of the Update Report is difficult to parse and adds limited value to the assessment. The revised example calculations in Annex 1 provide Vale's current understanding of wildlife risk in the woodlots and adjacent fields.

24. **Page 4.17. Section 4.2.5.** In this revised CBRA, Stantec changed their TRVs from the TRV's used in the previous version of this CBRA to the default MOE TRVs from O. Reg. 153/04 (MOE 2011). However, they did not consider if the default MOE TRVs are appropriate for this site or if they are based on the most up to date science. This is a requirement for all risk assessments submitted under the regulation and is especially relevant for a site-specific assessment within a CBRA. For example, for mammals, the original Ni TRV used by JWEL (2004) was based on a LOAEL of 30 mg/kg-day from a two-generation study with rats (Springborn 2000a). However, a re-analysis of this study conducted by the WHO (2005) results in a LOAEL of 2.2 mg/kg-day (based on post- implantation loss and perinatal mortality). CCME (2015) selected this analysis for deriving the human health based soil quality guideline. However, for mammals and birds, CCME used a TRV of 14.6 mg/kg-day based on a 44% reduction in growth in Holstein calves over an 8 week period. These lower values are based on more up-to-date science and are lower than the TRV used previously (30 mg/kg-day), the TRV used in the generic model (80 mg/kg-day) or the TRV used in this risk assessment under the Modified Ecological Protection option (152 mg/kg-day). A rationale is required for all TRVs to support their use in this risk assessment.

Vale Response: The Ministry's default TRV for mammals is based on the Ambrose et al. (1976) study, which was confirmed as the TRV to be used under the Ministry's Modified Generic Model in Nov. 2016. The original CBRA risk assessment used a TRV derived from the Springborn 2-generation reproductive toxicity study, but it was used incorrectly, the dose of $NiSO_4 \cdot 6H_2O$ being used rather than the dose of Ni contained in the nickel sulfate hexahydrate (NSHH) (the Ni content of $NiSO_4 \cdot 6H_2O$ is 22%). The LOAEL-based TRV would therefore be 2.2 rather than 10, as indicated in the original CBRA Natural Environment Ecological Risk Assessment.

The CCME's selected TRV is based on O'Dell et al. (1971) [J. Animal Sci. 32(4): 769-773]. This 49 year-old study is not new science. The problem with the O'Dell study is that the authors used nickel carbonate added exogenously to the food as a powder. It is well known that palatability due to the metallic taste of the added nickel salt is a deterrent to food consumption. This was seen in the Ambrose et al. (1976) [J. Food Sci. Technol. 13: 181-187] study as well, which dosed rats in a similar manner to O'Dell. Some of the reduced growth seen in the Ambrose study was also interpreted to be due to food palatability causing reduced food intake and reduced growth. It is for this reason that newer studies such as the Springborn 2-generation rat reproductive study use gavage dosing, since this removes the issue of food palatability which can act as an experimental confounder that can lead to reduced growth and potentially be misinterpreted as a sign of toxicity. TRVs based on the Ambrose study are more scientifically sound values than the O'Dell value that was surprisingly selected by CCME for the derivation of soil quality guidelines for Ni in Canada. In Annex 1, Vale has provided a revised ecological TRV based on the Springborn study.

25. **Page 4.18. Section 4.2.5.1. Modified Ecological Protection.** It is highly unusual to apply the modified ecological protection option for a large geographic area as done in this revised CBRA. The MEP approach was developed under O. Reg. 153/04 to minimize inappropriate risk management on a local scale (i.e., on individual properties); it was never intended to be used for a CBRA over a large geographic scale. It also has several conditions that need to be met and requires a certificate of property use to inform future land owners that adverse effects may occur to some plants, soil

organisms, and wildlife that might reside in or frequent the site. This option essentially treats the land as zoned industrial and uses less stringent eco-toxicity values to develop site-specific soil standards. In addition, risks need to be calculated with and without modified ecological protection. Overall, it is not acceptable to only use this approach for estimating risks to ecological receptors in this CBRA.

Vale Response: As discussed above, the MEP approach was used to assess risk for the wider area of Port Colborne, knowing that the contamination is widely distributed and the ecosystems seem to be generally functioning normally in terms of many ecological processes. For the contaminated woodlots of Port Colborne, as an example, appear to have impairment in decomposer pathways and invertebrate populations, yet the woodlots still appear to be more or less normal. The question for risk management has always been (during the CBRA process) whether to cut down the woodlots to remediate the soil metal contamination. It was thought, in earlier discussions, that remediation by cutting down woodlots and remediating the soil would be worse than the soil metal contamination itself. The use of MEP was an attempt to put a different lens on the issue.

Vale has recently begun re-examining the woodlot remediation issue, and current thinking is that the woodlots could be managed using selective silviculture methods to remove trees from areas with elevated metal concentrations, associated with hot-spot removal and replanting or natural recolonization by trees. Risk management activities need not involve the cutting down of entire woodlots. In addition, the impacted ecological processes such as decomposition functions, will be reassessed in the PCCAP to obtain additional knowledge to support or reject the previous view that the woodlots should be left alone.

26. **Page 4.18, second paragraph.** The objective of the risk assessment was not to identify those areas where remediation was or was not required.

Vale Response: Comment received. This was part of the objectives in a practical sense.

27. **Page 4.18, third paragraph.** Using the MEP approach is not a reflection of the "conservatism inherent in the standards". As noted, the main purpose of the MEP is to avoid inappropriate risk management activities that result in net environmental damage (e.g., removing terrestrial habitat by paving an area to limit exposure).

Vale Response: Comment received. Paving of a small industrial property is an obvious example for the use of MEP, but the Port Colborne situation is another unique example where some risk management activities could lead to net environmental damage, or at least no net gains of ecological integrity. Additional discussion on the use of MEP is provided elsewhere in the comment-response dialogue.

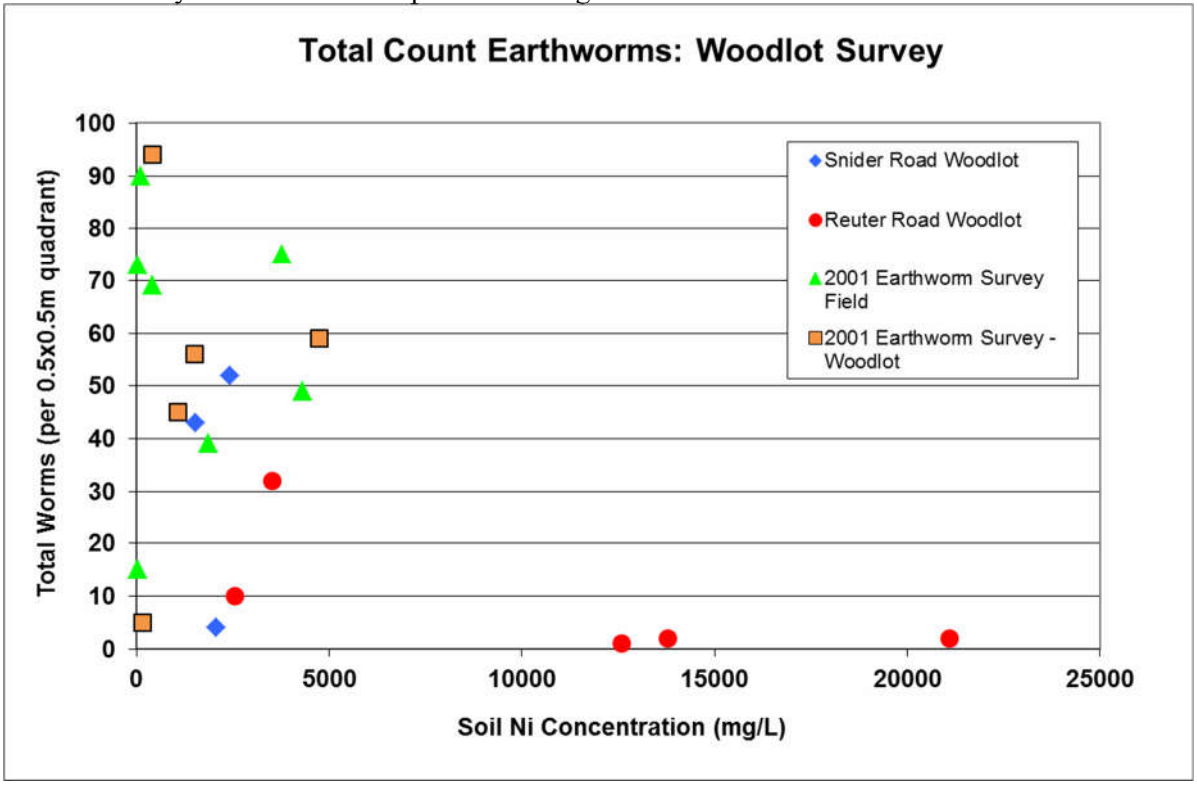
28. **Page 4.19. Section 4.2.5.2 Surface Water.** Aquatic Protection Values (APVs) have not replaced Provincial Water Quality Objectives (PWQOs). APVs can be used to better understand potential risks of elevated COCs in surface water but they should be used in conjunction with PWQOs.

Vale Response: Comment received. Ideally, bioavailability-based approaches to assess chronic aquatic risks would be used, as these reflect the latest scientific understanding of aquatic risk of metals such as Ni, Cu, and Co. Such an assessment will occur in the PCCAP.

29. **Page 4.21. Section 4.2.6.1. Assessment of Risks to Plants and Invertebrates**. Since these HQ were developed using the MEP option, a HQ of 4.7 does not represents a "marginal risk" to plants and invertebrates. Since limited site-specific information is available for herbaceous plants in woodlots and non-agricultural fields (other than the goldenrod data), information from the Crops ERA would be more appropriate for assessing risks to plants in woodlots and non-agricultural fields. Risks to invertebrates should be addressed separately. In addition, instead of a qualitative statement defining potential areas at risk, a spatial analysis should be provided that clearly identifies those areas where soil COC concentrations exceed a HQ of 1.

Vale Response: Comment received. A detailed spatial analysis of the Reuter Road woodlot (the topic of Section 4.2.6.1, given that the highest Ni concentrations were located there) should be possible following the PCCAP woodlot soil mapping work.

30. **Page 4.22, 3rd and 4th paragraph.** The presence of a few adult and/or juvenile earthworms at soil concentrations greater than 20,000 mg/kg does not indicate a "healthy earthworm population". While there is variability in total number of earthworms at lower concentrations, there are clearly adverse impacts to earthworms at elevated Ni concentrations (see MOECC Figure 1). The field results support the site-specific earthworm toxicity data of adverse impacts occurring at much lower soil Ni concentrations.



MOECC Figure 1: Relationship between Total Number of Earthworms and Soil Ni Concentration

Vale Response: Comment received. Clearly, that passage was inappropriate. Indeed, adverse effects have been identified and acknowledged elsewhere.

31. **Page 4.23, 3rd paragraph.** A well conducted field survey with the ability to detect

differences is needed to support the approach discussed in Chapman 2005.

Vale Response: Comment received.

32. **Page 4.24. Section 4.2.6.2. Assessment of Risks to Birds and Mammals.** MOECC does not consider the potential risk to mammals and birds to be irrelevant. Given the uncertainty over the estimated Average Daily Dose (from Section 4.2.4.3), and the use of inappropriately high TRVs using the MEP option, it is clear that many of the Hazard Quotients calculated for most of these VECs will exceed 1.0 under the worse-case scenario.

Vale Response: Comment received. See Annex 1 for a detailed response.

33. **Page 4.25. Table 4-14.** Risks to sheep in the adjacent field scenario will need to be based on an agricultural setting; not industrial as assumed under the MEP option.

Vale Response: Comment received. See new calculations provided in Annex 1.

34. **Page 4.26. Section 4.2.6.3. Assessment of Risks to Amphibians.** The assessment of risks to amphibians are only appropriate for the Wignell and Beaverdam drains but are limited by the fact that they are based on only one water quality sampling event from October 2013 and that the hazard quotients are calculated based on comparisons to APVs instead of PWQOs. As noted previously, total concentrations of COCs collected from these drains are much lower than the concentrations measured from the intermittent
ponds found in the primary and secondary area that were used in the risk modelling of other receptors (see Table B-4). Overall, despite the discussion provided on the frog calling survey, the CBRA is unable to discount that adverse impacts may be occurring to amphibians in some intermittent aquatic habitats. However, it is likely that the potentially impacted areas overlap with areas already identified as having an adverse impact based
on elevated COC levels in soils and impacts to other ecological receptors.

Vale Response: First, the current science regarding aquatic risk would use 0.45 µm-filtered samples and BLM-based risk assessment rather than total, unfiltered samples as required by the outdated PWQO approach. The original sampling of the aquatic environment in the CBRA was conducted in 2000-2002 and assessed risk using unfiltered water samples. This approach potentially overestimated risk and certainly did not underestimate risk. The additional sampling conducted by Vale at two sampling locations in the Wignell and Beaverdam Drains in October 2013 and included in the ERA chapter of the Update Report was intended to provide a link to the most up-to-date science via the use of BLMs for Ni, Cu, and Co. Second, the original analysis and that in the Update Report included samples from the primary study area which were actually from the current operating site, which is not subject to the CBRA. Samples S1-S3 in Table B-4 of Chapter 4 of the Update Report should not be included for assessing aquatic risk outside of the operating site.

35. **Page 4.27. Section 4.3. Conclusions.** There is no rationale provided to support the conclusion that the previous SSTLs developed by JWEL are valid. No analysis has been conducted to determine what the soil COC concentration would be at an HQ of 1.0 based on this revised assessment under the worse-case scenario for the woodlot and adjacent field habitat. Areas greater than the recommended soil thresholds should be identified to inform potential risk management measures.

Vale Response: Revised risk calculations for the woodlot and adjacent field scenarios are provided in Annex 1.

36. **Appendix B of Chapter 4**.
    a. **Table B-1**: It is not clear why the soil sample from LL17 was not included in this dataset. Regardless, the risk estimates based on the currently 95% UCLM is unlikely to change if this data is added.
    b. **Table B-2:** It is not clear why the soil samples from IH2 (Ni = 3,790 mg/kg) and IH4 (Ni = 2,600 mg/kg) are not included in this dataset while data collected nearby these samples are. As noted, the absence of these 2 datapoints may influence the 95% UCLM for the "worse-case" field environment.
    c. **Table B-3 and B-4.** A few sediment and surface water samples in the primary study area have much higher COC concentrations than the rest (e.g., sediment site FH3; surface water sites S2 and S3). These samples may be more representative of the worse-case scenario analysis since they appear to be located in or around Woodlot #3 (at least for sediment; not clear for surface water where samples are from).

Vale Response: Regarding (a), Sample LL17 should probably have been included (22,700 mg Ni/kg). Regarding (b) it is not clear why the consultant left these samples out of the analyses. Also, samples CS-H-7, CS-H-8, and CS-H-9 were all relatively low values and probably should not have been used to calculate the worse (sic) case (i.e., worst-case) UCLM values for the field environment. See Annex 1 for detailed response to these comments.

Comments on Chapter 5 – Ecological Risk Assessment - Crops

The following review comments are for the report titled *Port Colborne Community-Based Risk Assessment (CBRA) 2014 Update Report, Chapter 5 – Ecological Risk Assessment –Crops, prepared for Vale Canada Limited by Stantec Consulting Limited, Guelph, Ontario, File number 122210662, September 12, 2014* (Update Report). The update refers to updating the Crops Studies section of the CBRA conducted in the early 2000s (Jacques Whitford, 2004)[1]. Crop studies were conducted on Port Colborne soils in the field and in greenhouses in 2000 (referred to as JW 2000) and in 2001 (referred to as JW 2001). These studies were designed to determine the effects of arsenic, cobalt, copper and nickel in Port Colborne soils on selected crops. Nickel was targeted as the primary toxicant. The consulting firm Jacques Whitford Limited conducted these studies for Inco Limited. Although Vale (then CVRD) took over Inco in 2006 and Jacques Whitford became Stantec Consulting Limited in 2010, the primary authors of this chapter of the Update Report have been involved with the CBRA review and response process for years and one of the authors was lead scientist for the JW 2001 crop studies.

The following comments on the Update Report follow the sections given in Chapter 5 of the Update Report.

37. **Section 5.1** of the Update Report provides background information and states the purpose of the

[1] Jacques Whitford, 2004. Port Colborne Community Based Risk Assessment – Ecological Risk Assessment, Crops Studies, Project No. ONT34663. Prepared for Inco Limited by Jacques Whitford, December.

Crop risk assessment, which was to determine "*the concentrations in historically deposited COC in Port Colborne soil that represent an unacceptable risk (phytotoxicity) to agricultural crops*". The authors go on to give the purpose of the Update Report "B*ased on the multiple rounds of review and response, there were areas of disagreement between reviewers [of the CBRA Crop Studies] and the authors of the report. To this discussion, the MOE review is added, and this chapter of the 2014 Update Report is primarily a response to the MOE's review comments. It is hoped that the discussion below provides the necessary clarity to finalize the Crop risk assessment fourteen years after its initiation."* The MOECC understands that this has been a very long process, with multiple rounds of review and responses and considerable discussions on how best to move forward to address our concerns. While the update report has considered additional information from other crop studies conducted in the Port Colborne environment, the new analysis does not adequately reflect our previous concerns. As a result, the proposed SSTL's are exactly the same as the SSTL's in the original 2004 Crop Studies report (Jacques Whitford, 2004).

Although the 2004 Crops Report includes several studies, the SSTL values are based only on the JW 2001 greenhouse studies. As has been stated previously by the Ministry (MOE2011)[2], these studies are not considered definitive for several reasons including the lack of yield data, the growing of plants in a mix of soils other than agricultural soils (soils were collected from woodlot and railroad right of way), the growing of plants in pots, the growing of plants in a greenhouse rather than under field conditions, and the focus on only one crop (oats). The ministry recognizes that Vale has put considerable time and resources into conducting these studies, with the likely expectation that these studies would be definitive. Also, we acknowledge that when the JW 2000 study did not work out as expected, Vale was willing to fund a new upgraded study for the JW 2001 studies. The ministry understands that the development of SSTLs by Vale is a voluntary process and that conducting additional crop studies may not address limitations in the JW 2000 and 2001 studies. However, the ministry is also very aware of the historic concerns expressed by the Port Colborne agricultural community regarding adverse effects to crops attributed to emissions from the nickel refinery and high nickel and other metal concentrations in the area soils. The Ministry is also very familiar with many of the studies conducted in the Port Colborne area on the effect of nickel and other COCs on crops. In fact, several of these studies, as well as complaint investigations, were conducted by Ministry scientists. Consequently, the Ministry suggested in discussions with Vale after our comments were provided in May 2011 that it might be possible to develop more appropriate SSTL's incorporating not only the CBRA studies but also studies conducted on crops in soils from the Port Colborne area. We note that although the ministry has not recently received complaints regarding nickel toxicity in Port Colborne crops, this should not be interpreted as meaning that there is no longer a problem with soil nickel toxicity to agricultural crops in the Port Colborne area.

Vale Response: Comment received. The Ministry's comment identifies many of the problems faced by Vale (Inco at the time) as the new (at the time) CBRA process unfolded. Vale has been evaluating remedial options in earnest over the past five years, with field trials of agricultural liming (at 88 tonnes/hectare, as recommended in the Integration Report) on clay soil (crop yield was measured), some additional phytoremediation trials using <u>Alyssum</u> <u>murale</u> (lab only), and a deep tilling trial, work

[2] MOE 2011. Letter to Mrs. Maria Bellantino Perco (Senior Specialist, Environment, Vale) from Camilo Marinez (Coordinator, Community Based Risk Assessment, MOECC) providing ministry comments on Vale Port Colborne Community Based Risk Assessment.

completed under an NSERC Collaborative Research and Development Grant to Professor B.A. Hale at the University of Guelph (entitled "Remediation of Ni Toxicity by Liming – Field Validation") which followed-up on the earlier (year 2000 and year 2001) studies conducted for the CBRA. Vale has acted to respond to the Ministry's comments over the past few years by initiating new, further study to help manage the agricultural risks appropriately.

38. **Section 5.3** gives an overview of the JW 2000 and JW 2001 crop studies. For the JW 2000 study, the Update Report states *"Data generated from the 2000 Greenhouse Trials proved unsuitable for derivation of phytotoxicity thresholds due to confounding soil variables, analytical difficulties and (in some cases) an inappropriate range in soil CoC exposure concentrations* (Section 5.3.1, pg. 5). It is understood that Dr. Jim Warren was in charge of the JW 2000 studies and that while these studies were less than ideal, it is not clear whether Dr. Warren, the person in the best position to judge the merits of the studies, considered the 2000 data unsuitable. In the Crops Report and the Update Report, evidence of suppressed growth of corn, oats and soybeans from the JW 2000 studies at nickel concentrations at or close to 200 ug/g nickel (Tables GH-1, GH-2, GH-5, and GH-9) is largely ignored (Jacques Whitford, 2004) yet the Update Report uses the JW 2000 results to support conclusions regarding the suitability of the Port Colborne soils for crop growth, such as "*The result of the field trials conducted in 2000 were equivocal; however, they generally supported the tenet that crops could successfully be grown in soils greatly exceeding the MOE generic soil criteria for nickel*" (pg. 5.4). The Ministry acknowledges that there were shortcomings to the JW 2000 studies, but also recognizes that the results from these studies have some validity.

Vale Response: In the Update Report (Chapter 5, Appendix 5B, section 1.3.14), Vale reanalyzed the year 2000 greenhouse studies. In the original Crops ERA, this was not done. In response to the Ministry's 2011 comments, Vale specifically addressed these experimental results. Because of problems that occurred during the year 2000 greenhouse studies, these data were difficult to analyze and develop toxicity thresholds for. The only data from year 2000 used in the reanalysis in the Update Report, were the soybean data associated with organic soil. See section 1.3.14.1 of Appendix 5B of the Update Report. Vale believes that it has, in fact, conducted the analysis that the Ministry requested in its 2011 comments. Again, see Appendix 5B, section 1.3.14 of the Update Report for a clear explanation of the data analysis conducted by Vale.

39. As stated previously, a major shortcoming of the JW 2001 studies was the lack of yield data. This issue was never directly addressed in the Vale/Stantec responses to our previous comments on the crops study. However, this issue was also raised by the independent consultant peer reviewer (Watters, 2008[3]) and at that time, a response was provided (Jacques Whitford, 2009[4]). Although this response went into considerable detail explaining how there can be a relationship between biomass and grain production, using terms such as harvest

[3] Watters, 2008. Independent Consultant Peer Review Report for the Community Based Risk Assessment (CBRA) Ecological Risk Assessment on Agricultural Crops in Port Colborne, Ontario. Prepared for the Public Liaison Committee and City of Port Colborne by Watters Environmental Group Inc., Reference No. 04-0007, October 2008.

[4] Jacques Whitford, 2009. Commentary on Watters Environmental Group Inc. October 2008 Document – CBRA Crops Studies in Port Colborne, Ontario, Project No. ONT34657, Prepared for Vale Inco Limited, April 2009.

index and mentioning that "plant biomass is a standard measurement used in phytotoxicity studies" and that "the results obtained by using plant biomass data are reliable and comparable with other well documented scientific studies" (Jacques Whitford, 2009), it failed to address the key issue, which is that for the agricultural community, yield is critically important and yield of oats means the quantity of grain produced. It is understood that for some farmers, oat straw may be of interest and that oats may be used as a forage crop, but including a measure of the amount of grain produced is critical in any agricultural study looking at oat crops. Furthermore, Stantec has often used the term yield when referring to biomass of oats; this is not acceptable and should be changed in the reports. Trying to redefine the term "yield" does not change the fact that for an agricultural study with oats, the lack of any information on the amount of grain produced is a major shortcoming and a major source of uncertainly in the development of SSTLs from the JW 2001 greenhouse studies.

Vale Response: Vale recognizes that the Ministry's reviewer of both Chapter 5 of the Update Report and the original CBRA Crops ERA, remains dissatisfied with the use of the term "yield" regarding the bioassays using oats, in which above-ground plant biomass is the metric to which the term "yield" was attached. The response referenced in the Ministry's comment remains true. Harvest Index (HI) can be used to relate above-ground biomass to grain yield (see Lopez-Castaneda and Richards (1994) [Field Crops Research 37: 51-64] for an example of this usage) and clearly could be used to transform the data from the CBRA crops studies into a form that should satisfy the Ministry's review comments on this matter. Vale will not be making such data transformations, however. As mentioned in Vale's response to comment 37, in the past five years, Vale has been evaluating risk management options for agricultural crops, including phytoremediation, liming, and deep-tilling. The data generated in these field trials has been obtained in the form of yield measurements. Vale intends to consider these data with the earlier crop data generated under the CBRA process, and simply cannot accept that the data collected during the CBRA cannot be used and that the Ministry rejects the CBRA Crops Risk Assessment because yield was not evaluated, but only assessed phytotoxicity in terms of biomass.

40. **Section 5.3.2**. The relationship between soil and plant tissue concentrations of COCs in the greenhouse crops and the goldenrod collected as part of the Biomonitoring Study was considered to be similar and the report authors state that the Biomonitoring Study "greatly reduced the uncertainty regarding the legitimacy of the toxicity thresholds as calculated." This is similar to the wording used in the conclusions of the Biomonitoring Section of the CBRA Crop Studies report; yet in the results section of the Crop Studies report (3.0 Results) it is stated "the limitations of the experimental protocol, particularly the low replication of samples and lack of replication of sample sites within each treatment, restrict our ability to make generalizations regarding the COC uptake of goldenrods on different soils." (Jacques Whitford, 2004 – pg. 5-8). Viewing the data given in Appendix B-2 of the Crops Report, the latter appraisal is far more accurate than the former (i.e., there are significant limitations in the experimental protocol of the Biomonitoring Study and that the results do not "greatly reduce" the uncertainty as suggested). As can be seen in the data for the high sand plot (Plot 3) and the high clay plot (Plot 4), there is poor agreement between replicates of soil and plant tissue nickel concentrations (MOECC Table 1). Also, higher soil nickel concentrations do not necessarily mean higher plant tissue nickel concentrations (MOECC Table 1).

MOECC Table 1: Selected soil and goldenrod nickel concentrations from a sand and a

clay site as given in Appendix B-1 Data for Biomonitoring Study (Jacques Whitford, 2004)

Site	Plot	Replicate	Soil Ni (mg/kg)	Goldenrod Ni (mg/kg)
Sand	3	1	600	28.4
Sand	3	2	3440	28.1
Sand	3	3	4690	15.0
Sand	3	4	462	5.9
Clay	4	1	7267	8.8
Clay	4	2	6397	12.7
Clay	4	3	3583	12.4
Clay	4	4	3200	17.1

There are other weaknesses with the Biomonitoring Study which were pointed out in the Ministry's 2011 comments, including the assessment of only one plant species, the lack of separation of plant parts before chemical analysis, the differing ages and stages of development of the plant samples, and the lack of root data. Furthermore, the goldenrod is referred to as Solidago spp., which suggests that more than one species of goldenrod may have been sampled. It is possible that metal uptake and metal tolerance could vary by species. Also, goldenrod is a weedy species that is known to colonize well in heavy metal polluted areas (Dong et al., 2006[5]) and this plant can be considered a metal tolerant species rather than a good representative of Port Colborne flora. In summary, given the lack of replication, the uncertainty in what plant parts were sampled, the uncertainty as to the age and developmental stage of the sampled tissue, the lack of clarity on what species was sampled, the often high variability in uptake results, and the selection of a species known to tolerate highly metal contaminated sites, the argument that the Biomonitoring Study reduces the uncertainty of the calculated toxicity thresholds is not supported.

The MOECC understands that the contaminated organic muck soils in the vicinity of the refinery are currently owned by Vale and no longer in agricultural production. However, if these lands were sold, it is possible that they could be put back into agricultural production. Since it is not known what a farmer might try to grow on these lands or how a farmer might alter the soil chemistry though tillage practices, fertilization, liming, acidification or pesticide applications, it is important not to underestimate the phytotoxic potential of the nickel in these soils. It is important to remember that nickel toxicity in these soils is not a theoretical problem, since historically muck farmers have reported serious issues in growing crops on these lands that were attributed to soil nickel contamination.

Vale response: Vale agrees that potential future landowners should have the knowledge regarding potential environmental issues on the lands that they purchase. The public record being what it is, and given the legal obligations to disclose contamination of land offered for sale, it is difficult to imagine that Vale or any land owner could sell property without full legal disclosure of the soil contamination. Regarding the goldenrod biomonitoring study, there has been significant study on goldenrod reported in the literature since 2006. It may well be that goldenrod (Solidago canadensis) is a highly suitable plant species for biomonitoring. Immel et al. (2012) [J. Proteom. 75: 1129-1143] provides one example of such recent research. It has been found that goldenrod is likely a highly suitable biomonitoring plant species, with proteomic responses including up- and down-regulation of

[5] Dong et al., 2006

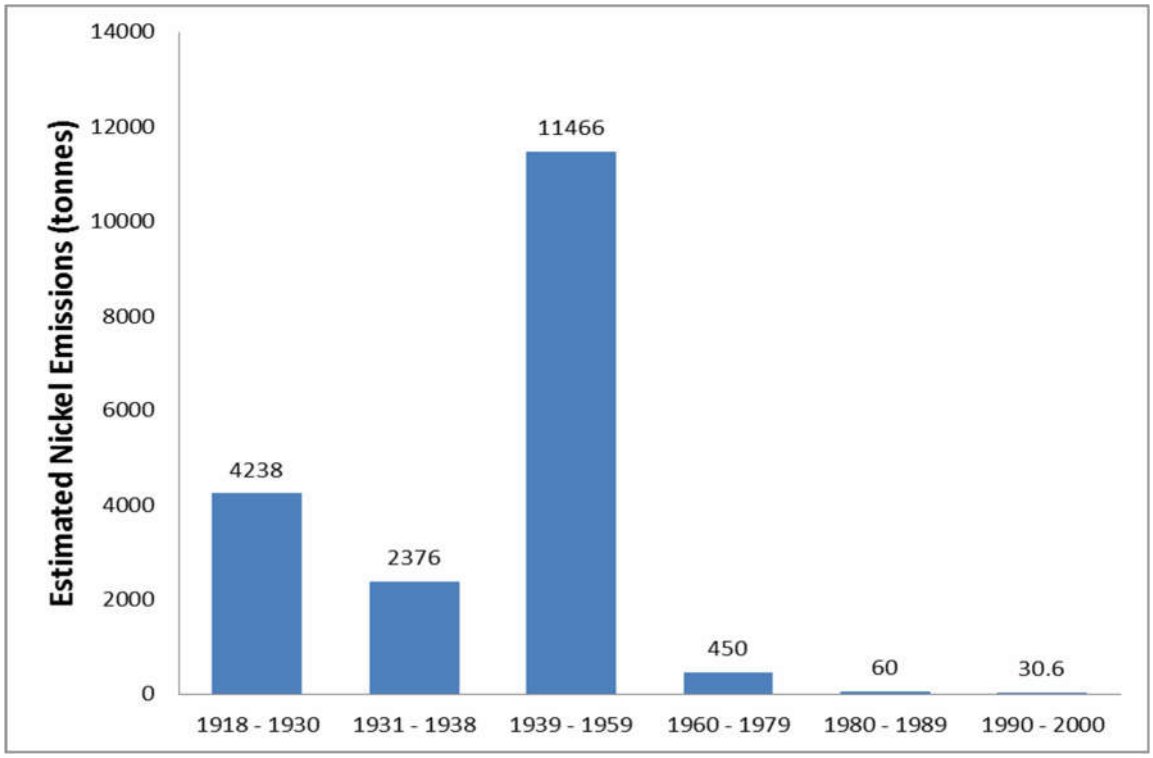
a large number of proteins indicative of stress. Goldenrod also has complicated environmental interactions, including allelopathy, promotion of soil microbial biomass, microbial functional diversity, nitrogen fixation, increase in soil pH, soil bulk density, and pathogen suppression.

41. **Sections 5.4 and 5.5 (including the various subsections).** Stantec identifies the MOECC concerns, outlines a strategy to resolve the issues and provides a meta-analysis of the data. It is important to note that the MOECC, Stantec and Vale were initially working through this process together but that Vale ended the consultative process and the MOECC was not involved in the final meta-analysis of these studies. As with any meta-analysis, the decisions to include or exclude data are critical to the outcome and the ministry was involved with and agreed with the inclusion/exclusion decisions and score assigned to each study. Our concern rests with how the meta-analysis was used to support the SSTLs developed in the JW2001 document rather than as the basis for the development of new SSTLs based on all Port Colborne crop studies.

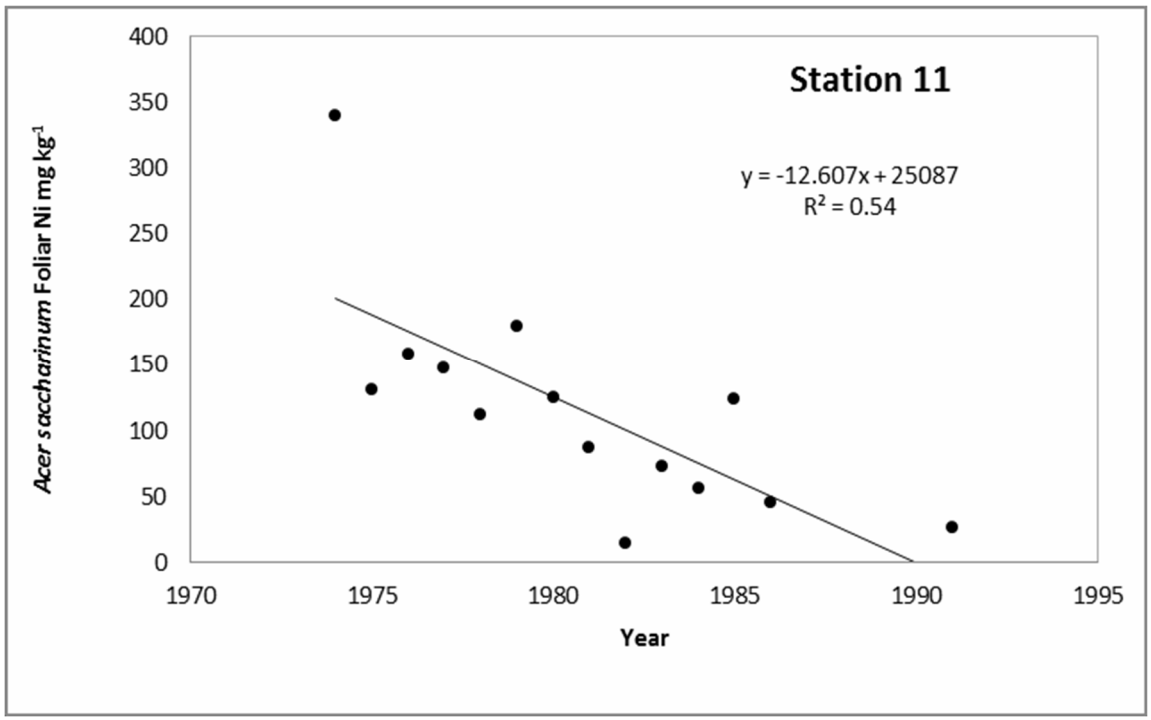
    In Section 5.5, the Update Report mentions studies dating back to the 1950s, and points out that when the nickel refinery was in full production that there was a significant amount of nickel, possibly water soluble, deposited on local vegetation and soils, which resulted in phytotoxicity. It is important to note that the amount of nickel emitted and the composition of refinery emissions changed dramatically after an electrostatic precipitator was installed at this refinery in 1961. Prior to this installation, the refinery operated largely without pollution controls and approximately 97% of the nickel emitted from the refinery from 1918 to 2000, occurred prior to 1960 (MOECC Figure 2). Given the drastically different levels of pollution in the Port Colborne area from the 1950s to late
    1970s, the ministry does not consider it appropriate to refer to studies conducted on the
    1950 in order to downplay the importance of nickel uptake from the soil in studies conducted from the late 1970s to early 2000s.

    The Update report also makes the argument that the refinery was still in operation when many of the complaints were made by local farmers and that nickel concentrations in local vegetation were much higher when the refinery was in operation than after it shut down in 1984. The authors show a graph of nickel in unwashed silver maple foliage from the late 1950s to 2001 (Figure 5-1), which shows a steep decline in nickel concentrations with time. The authors state that this "points to the importance of active emissions to nickel accumulation and toxicity of silver maples" and that "The same trend would apply to agricultural plants" (page 5.11). While this may seem reasonable, the argument is not supported when stations closer to affected farms are considered. The data given in Figure
    5-1 is for MOE Station 11, yet it is MOE Station 14 that is adjacent to two muck farms where many of complaints and MOE investigations and studies were conducted (MOE,
    1979).

    When comparing nickel concentrations in unwashed silver maple foliage collected by the MOE at Stations 11 with Station 14 from 1974 to 1991, it is clear that Station 11 has much higher foliar nickel concentrations and that the decrease in foliar nickel concentrations is much more pronounced at Station 11 than at Station 14 (MOECC Figures 3 and 4).

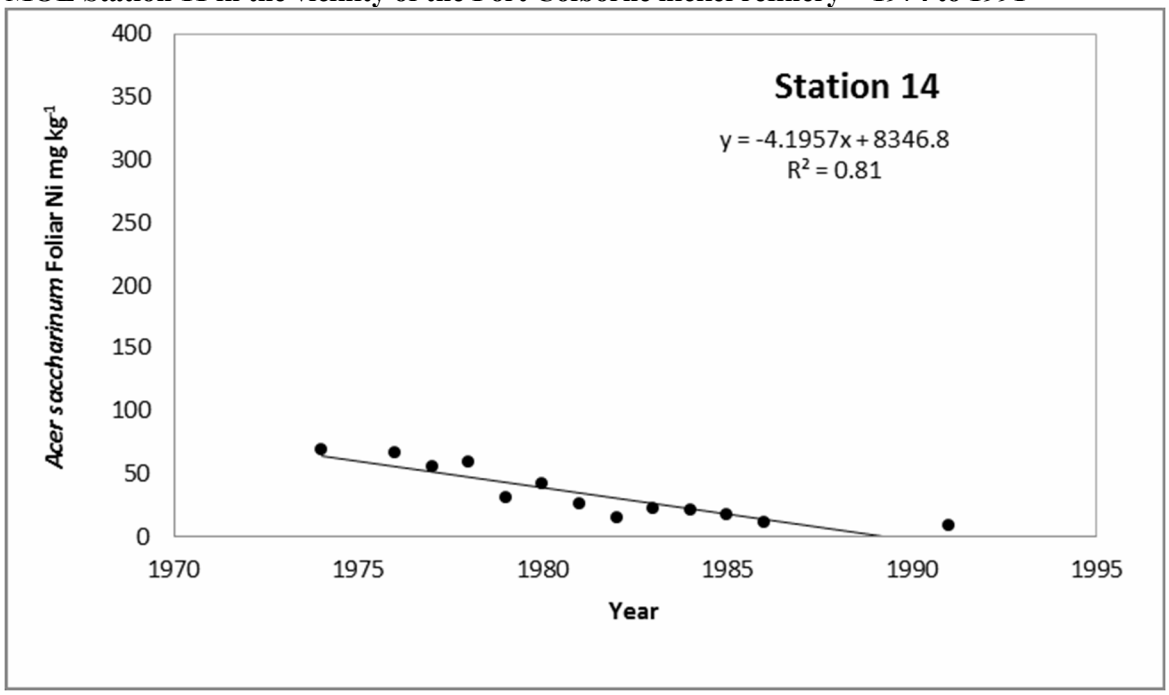


MOECC Figure 2: Estimated nickel emissions (tonnes) from the Port Colborne refinery from 1918 to 2000 (JWEL, 2001c)



MOECC Figure 3: Nickel concentrations in silver maple foliage (ug/g dry weight) from

MOE Station 11 in the vicinity of the Port Colborne nickel refinery – 1974 to 1991



MOECC Figure 4: Nickel concentrations in silver maple foliage (ug/g dry weight) from MOE Station 14 in the vicinity of the Port Colborne nickel refinery – 1974 to 1991

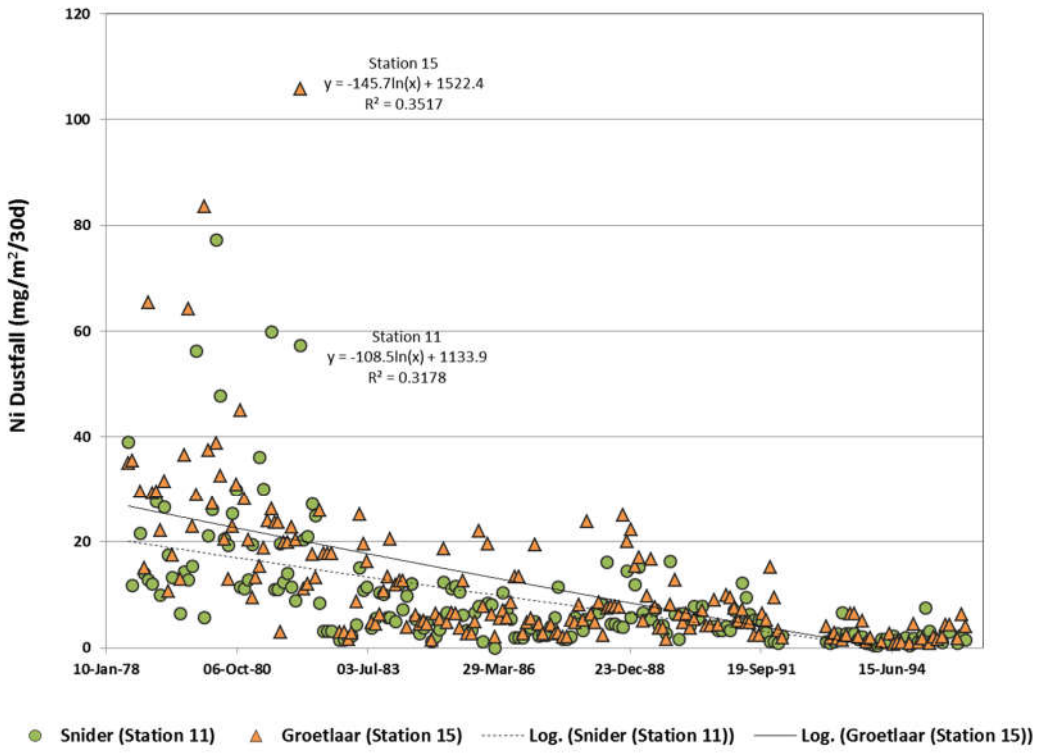
It is acknowledged that aerial deposition of nickel onto tree leaves can cause injury to leaves, but this should not be over-stated. In the late 1970s when injury to silver maples leaves was noted in the vicinity of Christmas and Killaly Streets (850 m northeast of the refinery), nickel concentrations in unwashed maple foliage at these sites were as high as 309 ug/g (MOE, 1977). This concentration is approximately double the foliar nickel concentration observed at Station 11 (MOECC Figure 3) and over four times higher than the foliar nickel concentration at Station 14 (MOECC Figure 4) over the same time period. Also, nickel in particulate on the leaf surfaces may not be available for plant uptake and the particulate can be washed or blown from the leaves by precipitation and high winds before it affects the foliage. Furthermore, the nickel toxicity was noted in plants grown in the Port Colborne muck soils even when there was no particulate on the leaf surfaces from Inco emissions. The "bioassay experiments" conducted on muck soils from the farms around Station 14 by the Ministry in the 1970s were conducted in greenhouses in Toronto, well away from any influence from the Port Colborne refinery emissions. This means the phytotoxicity documented in this study was from soil uptake of nickel and not from aerial deposition of nickel (MOE, 1978)[6]. Although the Update Report downplays the relevance of studies conducted before 1984, with statements such as "some caution is required when comparing the toxicity of nickel in Port Colborne soils from the period before 1984 with the toxicity of the nickel in soil today" (pg. 5.13), the Ministry considers these studies still relevant today and that less caution in accepting the relevance of these studies is required than suggested. Again, it should be noted

[6] Although root-knot nematodes were found to cause significant growth reductions in lettuce and celery grown in these muck soils, metals in these soils were calculated to reduce lettuce growth by 20-35% and celery growth by 30-35% (MOE, 1978)

that the vast majority of the nickel in these soils was deposited prior to 1960 and that this nickel had at least 15 years to equilibrate with the soil before the earliest of these MOECC bioassay studies were conducted.

Vale response: Vale suspended the consultation process with the Ministry due to the inability to bridge the gap over the TRV issue in the HHRA. Vale acknowledges that there were inadequacies in the CBRA process, which was a new process for Vale (Inco), the Ministry, and Ontario when it began in the year 2000. Vale recognizes that some of the CBRA studies which were used to generate data to inform the risk assessments could have been done differently, particularly when compared to current scientific practices. With each passing year, the studies appear more dated, as there are gains in the body of scientific knowledge. Nevertheless, there are some basic points of contention between the Ministry's review and Vale's understanding of the issues mentioned in its comments.

Regarding this particular comment, the point being made in the Update Report was that the Ministry had been focusing on studies conducted while Ni emissions were still occurring from the refinery, and considering that those studies conducted during that time period should be considered equivalent to those studies conducted in a time period that was more than 15 years after refinery atmospheric Ni emissions essentially ceased. This is not to say that



these studies conducted by the Ministry and others during the several years before closure of the Ni Refinery were not necessarily good studies, but rather, that the source of Ni being added to the agricultural fields near the Refinery included an "un-aged" or fresh component in addition to the

"aged" component of the soil Ni. Vale contends that this un-aged component no longer exists. The figure immediately above demonstrates that at Station 11 and Station 15, in the years prior to closure (1978-1982) the emission levels were higher than in the years from Refinery closure until 1991, when the effect of Refinery closure could be seen in the dustfall data. Vale's point is only that some of the studies conducted by the Ministry in the period around 1978 would have included a proportion of Ni that would have been more bioavailable, and hence more toxic than the aged Ni in the same soil, due to the presence of soluble Ni in the emissions, as discussed in the Update Report. Vale considers that the numerical values from these earlier studies should be viewed with this consideration in mind as part of the overall weight of evidence.

42. **Section 5.6.2.** This section considers other studies that have been conducted since 2004. Studies were conducted from 2005 to 2007 by growing oats and soybean on clay soils by a master's student under the supervision of Dr. Bev Hale of the University of Guelph. Yields of oats were poor and the Ministry agrees with the authors of the Update Report that it is difficult to make "specific conclusions as to the impact of the soil metal contamination on oat growth and yield" (pg. 5.17). Soybean yield was better, but variable from year to year. The Ministry agrees that it is not clear to what extent soybean grown in the Port Colborne clay soils are being affected by soil nickel concentrations. In August 2010, Vale arranged for a site visit for the MOECC to a farm northeast of the refinery where there appeared to be a good soybean crop growing, in spite of elevated soil nickel concentrations. It should be noted that this site visit was not an assessment of a field study but simply the observation of a soybean crop grown on contaminated land by an area farmer. From this brief visit it was not clear how the soil chemistry had been altered by the farmer through liming and fertilization or how soybean yield had been affected by the various soil nickel concentrations across the field.

Vale response: Comment received. A paper from the Cioccio thesis has now been published. The citation is: S. Cioccio et al. 2016 Environ. Toxicol. Chem. DOI: 10.1002/etc.3634.

43. **Section 5.6.2.** There is considerable discussion regarding various soil extracts in this section, with the conclusion that strontium nitrate, calcium chloride, or aqueous extractants offer the most information. The use of various soil extractants can help to determine the availability of nickel to plants growing in these soils and possibly other organisms. The authors conclude that "*the long-term management of the agricultural lands affected by nickel contamination at Port Colborne will need to balance production and nickel translocation into crops"* (pg. 5.20). The Ministry agrees with this statement and no specific comments are warranted for this section. In terms of the availability of nickel in the Port Colborne soils and the translocation of nickel into crops, it should be noted that Vale put considerable resources into investigating the potential of plants, such as Alyssum murale and Alyssum corsicum, to extract nickel from these soils (Chaney et. al., 2003). This research showed that some plants can hyperaccumulate nickel from Port Colborne soils even in the 2000s, which is direct evidence of nickel translocation into plants.

Vale response: Comment received. Ni can be translocated into plants from soil, particularly in hyperaccumulator species.

Comments on Chapter 6 – Summary of Conclusions in CBRA

44. We recognize that Vale has spent considerable effort to update the CBRA to address our previous comments. However, despite these revisions, the ministry continues to have numerous concerns with the Port Colborne CBRA reports and the proposed Risk-Based Soil Concentrations (RBSC) (also referred to as site-specific threshold levels, SSTLs). Overall, we are unable to endorse the current CBRA or support the proposed RBSC's.

Vale response: Regarding Human Health, Vale believes that the Ministry has selected an inappropriate TRV for the human health risk assessment, as discussed throughout this comment-response dialogue and Annex 2. Vale could accept the majority of Ministry comments related to the HHRA other than the TRV issue.

Regarding the Natural Environment and Crops Assessments, Vale believes that the Update Report and original CBRA Crops Risk Assessment have appropriately identified thresholds for risk management and is proceeding to evaluate risk management options, including liming, deep-tilling, and phytoremediation. These options have been evaluated in a recently-funded NSERC Collaborative Research and Development (CRD) Grant, as mentioned elsewhere in the comment-response dialogue.

Vale is undertaking an assessment of Ni in the waters of the Wignell and Beaverdam Drains.

Vale is undertaking further study of the need for risk management options for woodlots east of the Refinery.

Appendixes Providing Detailed Comments on the Human Health Risk Assessment Component of the Revised CBRA

Appendix A: Toxicity Reference Value (TRV) for Nickel

Overall Conclusions on Oral Ni TRV:

The ministry does not support the Nickel (Ni) toxicity reference value (TRV) used in the revised CBRA for assessing oral Ni exposure. A TRV is the benchmark used in risk assessment as an indicator of the maximum acceptable daily dose to which a person may be exposed without adverse effects. The oral Ni TRV of 20 micrograms per kilogram body weight per day (µg/kg- bw/day) used in the CBRA is based on adverse changes in body weight and organ weight observed in exposed test animals (rodents). This TRV was originally supported by the MOECC as noted in previous ministry comments (MOE 2011). However, based on the most up-to-date scientific information, changes in weight are no longer the most sensitive endpoint to use in assessing oral Ni exposure. Instead, the MOECC supports a TRV of 11 µg/kg-bw/day based on adverse reproductive and developmental effects observed in rodents.

A number of considerations support the ministry's decision that 11 µg/kg-bw/day is the appropriate Ni TRV to use. This TRV was derived from studies where oral exposure to Ni was associated with increased post-implantation and perinatal lethality (i.e., effects on the developing fetus). In addition, this TRV is also appropriate for protecting adverse effects of Ni exposure on the male developing reproductive tract (i.e., effects in both toddler and adult males). Although this TRV of 11 µg/kg-bw/day was used in the CBRA in the sensitivity analysis, its application was limited to the adult receptor of reproductive age. In contrast, because of the concerns associated with Ni and adverse effects to the developing fetus and reproductive system in males, the MOECC supports using this TRV for both the adult and toddler receptor.

Nickel is also associated with oral provocation of dermatitis in humans. This effect has been observed in a study where Ni sensitized individual's experienced systemic dermatitis after ingesting a single oral Ni dose of 12 µg/kg-bw (Nielsen et al., 1999). This effect has also been observed at lower doses as well. Given the fact that this adverse effect of Ni exposure was observed in a human study, the MOECC considers (at the very least) an exposure dose of 12 µg/kg-bw/day as an upper limit for establishing an oral Ni TRV.

Overall, the TRV of 11 µg/kg-bw/day is considered by the MOECC to be appropriate for the protection of Ni-associated reproductive and developmental adverse effects including the potential toxicity of Ni in developing male reproductive organs in toddler and adult males. However, it is noted that this oral TRV may not be fully protective of Ni-sensitized individuals from provoking dermatitis. Finally, this TRV of 11 µg/kg-bw/day is supported by Health Canada (2010), the World Health Organization (WHO, 2007), the Office of the Environmental Health Hazard Assessment, California Environmental Protection Agency (OEHHA, 2012) and the analysis by EFSA (2015). This TRV represents the most up-to-date value to use in risk assessment as an indicator of the maximum acceptable daily dose to which a person may be exposed without adverse effects.

As described in more detail below, the recommended TRV of 11 µg/kg-bw/day is based on the

following:

1. The previous TRV of 20 µg/kg-bw/day based on changes in body and organ weight is no longer appropriate.
2. The TRV of 11 µg/kg-bw/day, based on developmental and reproductive effects, represents the most up-to-date science and uses the most appropriate endpoints.
    - It is supported by Health Canada (2010), WHO (2007), OEHHA (2012) and the analysis by EFSA (2015),
    - and is protective of effects on the male reproductive system for both adult males and toddlers
3. Oral provocation of Ni dermatitis in humans has been measured at a dose of 12 µg/kg- bw.
    - The TRV of 12 µg/kg-bw/day should be applied as an intake dose; not an uptake dose.

Vale Response: The question as to which TRVs are the most appropriate for assessing human health risks is probably the single most important aspect of the CBRA risk assessments, because the selection of a TRV can lead to very disparate conclusions concerning the level of health risk present in Port Colborne. The use of the TRV (11 µg/kg/d) derived by the Danish EPA or the TRV derived by the European Food Safety Agency (2.8 µg/kg/d) lead to the conclusion that even background (baseline) exposures to Ni from a typical Canadian supermarket diet (an average Ni intake of 11.1 µg/kg/d for children 1 to 4 years as per the Health Canada Total Diet Survey – 2000 – 2007 (HC, 2007)) represents an unacceptable health risk. In this response to comments, Vale's interpretation, which it considers to be completely transparent and scientifically valid , is presented in Annex 2.

Detailed Comments on Oral Ni TRV Selection:

1) ***The previous TRV of 20 µg/kg-bw/day based on changes in body and organ weight is no longer appropriate***

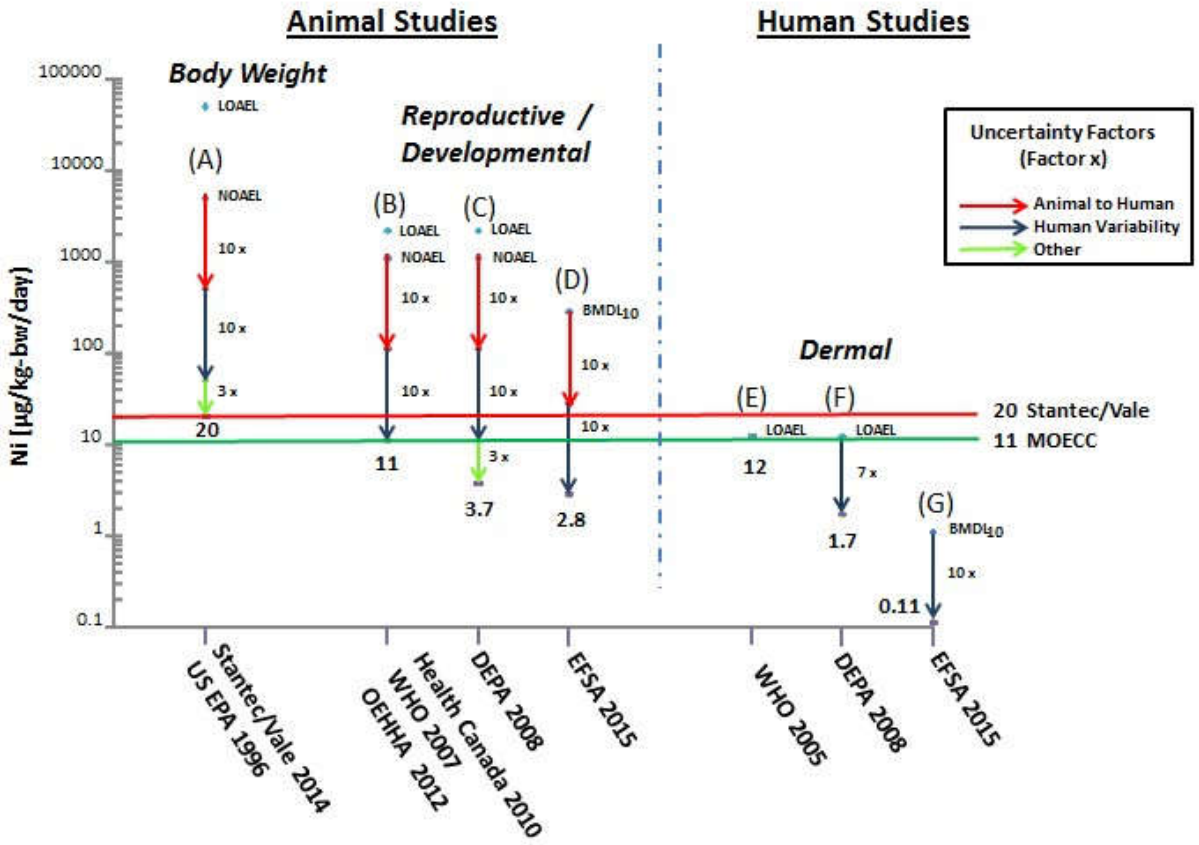
Stantec used a TRV of 20 µg/kg-bw/day from Ambrose et al. (1976) to evaluate oral exposure to Ni as part of developing risk based soil concentrations (RBSC) for the Port Colborne CBRA (see TRV "A" in MOECC Figure A1). This TRV was originally supported by the ministry at the onset of the CBRA review (2011). However, during the extensive consultation process (over several years) since our original comments were prepared, new toxicological assessments of Ni and Ni TRVs have been published. Consequently, the MOECC conducted a thorough review of all the new information on Ni toxicology and concluded that the TRV of 20 µg/kg-bw/day can no longer be supported.

The TRV used in the Port Colborne CBRA is the 1996 US EPA reference dose (RfD) for Ni based on a two year study in which rats were exposed to Ni sulfate (a water soluble form of Ni) spiked in their feed. From this study, a No Observable Adverse Effect Level (NOAEL) of 5 mg/kg/day was identified as the Point of Departure (POD) based on decreased organ and body weight (Ambrose et al., 1976). The TRV was derived by the application of a combined uncertainty factor of 300: 10 to account for intraspecies variability, 10 for interspecies variability, and 3 for inadequacies in reproductive studies to the NOAEL. At higher Ni doses, Ambrose et al. (1976) observed changes in body and organ weight but also observed increased lethality rates in the exposed animals. The low survival rate in the study, particularly in the control group, was criticized by both the California EPA (Cal EPA chRD, 2005; OEHHA 2012) and WHO (WHO DW, 2011) as a source of uncertainty in relying on this study to derive a TRV.

Although an uncertainty factor of 3 for inadequate reproductive studies was incorporated into the TRV derived from the Ambrose et al. (1976) study, there are other reproductive studies (e.g. Springborn, 2000a,b and Smith 1993) that were either not available or not considered by US EPA at the time of establishing its RfD. These reproductive studies have observed adverse effects at levels lower than the NOAEL of 5 mg/kg-bw/day reported in the Ambrose et al. (1976) study.
The Lowest Observable Adverse Effect Level (LOAEL) from these studies is plotted in MOECC Figure A1

MOECC Figure A1 illustrates the different TRVs considered in this review; the points of departure (PODs; LOAEL, NOAEL or $BMDL_{10}$) as well as the uncertainty factors applied to the POD (x = times) are included.

MOECC Figure A1 Ni Oral TRVs



In summary, adverse reproductive and developmental effects may occur at lower levels of oral exposure to Ni than adverse changes to body and organ weight. Therefore, changes in body and organ weight cannot be considered as the most representative toxicological endpoint for establishing a TRV for oral Ni exposure. As a result, the TRV of 20 µg/kg-bw/day that was used in the Port Colborne CBRA is out-of-date and no longer supported.

Vale Response: The CBRA HHRA was based on the "Ambrose" TRV 20, but Haber et al. (2017)

undertook a new derivation of a TRV for non-cancer Ni risk based on the Springborn 2-generation reproduction study using the preferred benchmark dose (BMD) approach and determined that the numerical value of the most sensitive (reproductive) endpoint is 20 µg/kg/d. A detailed discussion is provided in Annex 2.

2) The TRV of 11 µg/kg-bw/day based on developmental and reproductive effects represents the most up-to-date science and uses the most appropriate endpoints.

In the CBRA update report, the TRV of 11 µg/kg-bw/day was considered in the sensitivity analysis for assessing exposure to an adult of reproductive age. However, the MOECC supports using this TRV for the main analysis as it is based on the most up-to-date science and appropriate endpoints (reproductive and developmental effects), and is applicable to the toddler receptor.

Vale response: The rationale for applying a TRV (of 11 µg/kg/d) to adults (specifically to females of reproductive age) was that the Springborn 2-generation study administered the dose to female rats, so that any potential reproductive toxicity was conferred upon offspring via their mothers, first in the womb, and later via milk. The reproductive effects are not relevant to toddlers, who are prepubescent. It is noted that no developmental effects in rats were observed in the definitive 2-generation Springborn study (SLI, 2000b). Refer to Annex 2 for further discussion.

TRV of 11 µg/kg-bw/day is supported by Health Canada (2010), WHO (2007), OEHHA (2012), and analysis by EFSA (2015).

The TRV of 11 µg/kg-bw/day (see TRV "B" in MOECC Figure A1) is supported by Health Canada (2010), WHO (2007), OEHHA (2012) and the analysis conducted by EFSA (2015). This TRV is based primarily on the Springborn (2000 a,b) studies that identified an increased rate of post-implementation loss and perinatal lethality in rats treated by gavage with nickel sulfate (hexahydrate) in drinking water. The TRV was derived from a NOAEL of 1.1 mg/kg-bw/day and the application of a combined uncertainty factor of 100: 10 to account for intraspecies variability, and 10 for interspecies variability.

Vale response: It is imperative to recognize that the Springborn studies (i.e., the dose range-finding study (SLI, 2000a) and the definitive 2-generational study (SLI, 2000b)) did not identify an increased rate of post-implantation loss and perinatal lethality (PPL). It was an analysis of the Springborn data by regulatory agencies that identified the NOAEL for PPL to be 1.1 mg/kg/d. How these agencies appear to have come to the conclusion that the NOAEL for PPL was 1.1 mg/kg/d is discussed in Annex 2.

Vale's overall assessment is that the rationale used by other regulatory agencies to support a NOAEL for PPL (of 1.1 mg/kg/d) largely reflects superficial review and some degree of mis-citation or rubber-stamping of the regulatory literature, which was serially perpetuated by each additional regulatory agency in the citation chain. This is discussed in detail in Annex 2.

The NOAEL of 1.1 mg/kg-bw/day was identified based in part on the fact that an unbounded LOAEL of 2.2 mg/kg-bw/day was observed from the first generation range finding study (Springborn 2000a) (i.e., no NOAEL could be developed from this study alone). The analysis conducted by OEHHA

(2012) supported the NOAEL of 1.1 mg/kg-bw/day from the Springborn studies, and considered the Smith et al. (1993) study that independently identified a LOAEL of 1.3 mg/kg-bw day as supporting evidence. In addition, the CBRA report identifies the dose of 2.2 mg/kg-bw/day as a LOAEL for reproductive effects, relying on an independent analysis conducted by Seilkop (2013).

Vale response: Vale has great respect for Steve Seilkop, and his analysis provided in Seilkop (2013) is honest and well thought out. However, Vale's understanding of the basic scientific principles underlying DEPA's approach has continued to develop, and Vale now believes that a less complicated approach exists to assess the results of the Springborn studies. This is discussed in detail in Annex 2.

DEPA (2011) also considered the NOAEL of 1.1 mg/kg-bw/day based on the identification of a LOAEL of 2.2 mg/kg-bw/day from the combined post-implantation loss and perinatal lethality from the Springborn (2000b) study. DEPA's re-analysis considered that there was a mechanistic basis to assume that the effects on the developing fetus appear to be the same. This POD for reproductive and developmental effects was supported by WHO (2007) and Health Canada (2010). However, DEPA determined a TRV range of 3.7 to 5.5 µg/kg-bw/day after applying a combined uncertainty factor of 200-300: 10 to account for intraspecies variability, 10 for interspecies variability, and 2-3 for severity of effects observed at only twice the dose level of the NOAEL (see TRV "C" in MOECC Figure A1). Upon considering the rationale provided by DEPA (2011), the MOECC does not support the use of an additional uncertainty factor of 2-3 for severity of effects.

Recently, the European Food and Safety Authority (EFSA, 2015) reanalyzed the first generation range finding study (Springborn 2000a) and the subsequent full 2-generation study in rats (Springborn 2000b), combining the results from the two studies. EFSA identified reproductive and developmental toxicity as the critical effects for the risk characterization of chronic oral exposure to Ni, and derived a benchmark response at 10% extra risk (BMD_{10}) of 0.76 mg/kg-bw/day) with a lower 95th confidence limit ($BMDL_{10}$) of 0.28 mg/kg-bw/day), based on post-implantation loss of the combined single data set. Using the derived $BMDL_{10}$, EFSA estimated a tolerable daily intake (TDI) of 2.8 µg/kg-bw/day upon the application of a combined uncertainty factor of 100: 10 to account for interspecies differences, and 10 for human variability (see TRV "D" in MOECC Figure A1).

The MOECC agrees with the approach used by EFSA 2015 of combining the two Springborn rodent studies (2000a,b) and using of benchmark dose response analysis for deriving a TRV. However, the MOECC considers that the application of a total uncertainty factor of 100 to a $BMDL_{10}$ is tending towards an overly conservative consideration for use in the Port Colborne CBRA. For example, the use of BMD_{10} instead of $BMDL_{10}$ would yield a TRV of 7.6 µg/kg-bw/day instead of 2.8 µg/kg-bw/day.

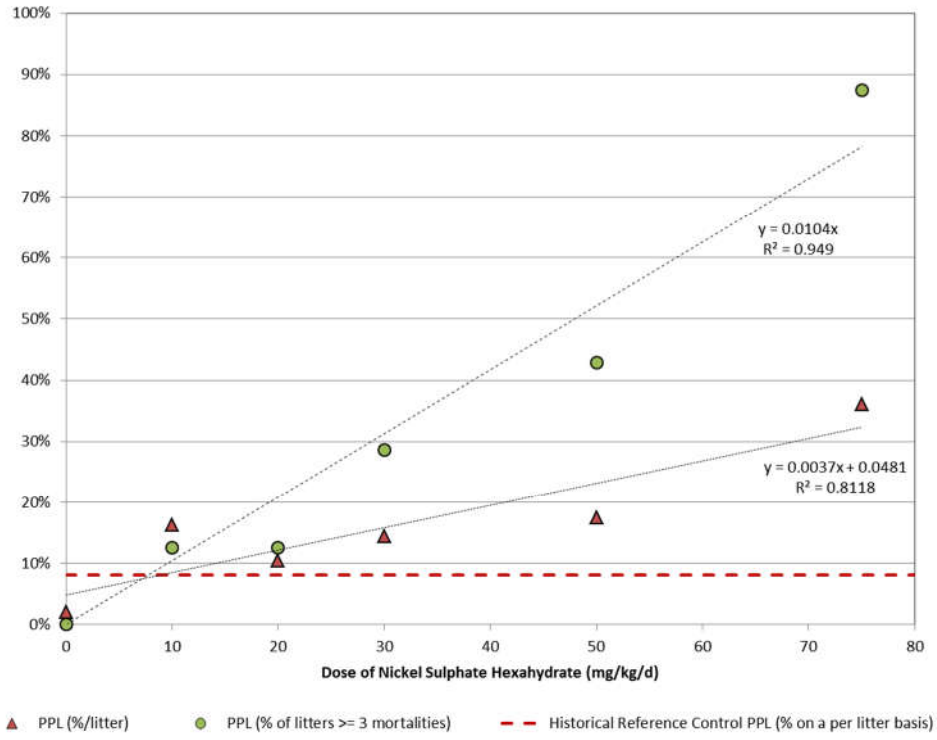
Vale response: EFSA's 2015 BMD analysis is inappropriate. The Benchmark Dose (BMD) approach is a regression approach that was conceptualized as a replacement for the conventional NOAEL/LOAEL approach. The NOAEL/LOAEL approach essentially compares the toxicological response at each dose and compares it with the response in control animals receiving no toxicant exposure. The NOAEL is the highest dose for which the toxicological response is not significantly different from that seen in the control animals. The LOAEL is the lowest dose for which the toxicological response is significantly different from that seen in the control animals. The NOAEL and LOAEL are independent of the toxicological responses observed at other dose levels. In contrast, the Benchmark Dose approach is intended to use the entire range of the dose-response data to develop statistical relationships

between the toxicological response and the corresponding doses, and for this reason, is preferred, scientifically. In theory, when sufficient data are available, the BMD approach is preferred over the NOAEL/LOAEL approach as the entire range of dose-response data is considered in a statistical manner.

EFSA's analysis has several errors, in Vale's opinion. First, the response metric commonly used for PPL is expressed as a percentage. This is because litter sizes are variable, as is the rate of PPL. For example, if there are 2 cases of PPL in a litter of 8 pups and 2 cases of PPL in a litter of 14 pups, the rates of PPL are 25 and 14%, respectively. What initially seems to be a similarity (2 cases of PPL) is actually seen to reflect important differences between the rates of perinatal mortality in the litters (those 2 failed cases of reproduction represent different rates of 25% and 14% PPL, which must be reflected in the analysis).

It must be noted that PPL is a natural phenomenon. Reproduction in vertebrates does not occur with complete fidelity. There is a natural rate of reproductive failure seen in mammals. This includes miscarries, resorptions, still births, and deformities, which occur at low rates in the absence of toxicant exposure. In the Sprague Dawley rats used in the Springborn 2-generation reproductive toxicity study, for example, the baseline rate of PPL in control animals is approximately 8% (8.13% as per Lang, 1993). This baseline rate of PPL among female rats (of 8%) was obtained from 3,541 dams (control female rats not exposed to any toxicant) from a total of 209 individual studies.

As previously mentioned, Vale is of the opinion that EFSA made two errors in its analysis. The metric for PPL was only considered on an absolute basis, not as a percentage of litter size. EFSA considered that baseline PPL occurred at an average rate of 2.3 per litter. As a result, EFSA developed the metric for its BMD analysis as the "number of litters with 3 or more instances of PPL" (since it is not possible to have 2.3 animals in an actual litter, EFSA rounded up to 3). This selected metric for PPL fails to use the entire range of dose-response data, contrary to the general goals for the BMD approach, and it also alters the dose-response relationship, as seen in the figure below.



For clarity, this figure considers the data from the Springborn dose range-finding (DRF) study (SLI, 2000a) only. It can be seen that by changing the metric for PPL from "percent PPL" on a per litter basis to "percent of litters with 3 or more cases of PPL", the slope of the dose-response curve is increased by roughly three times (from y=0.0037x to y=0.0104x in the figure above). This change in slope caused by EFSA's data transformation has the effect of making the 5% or 10% levels of increased risk from baseline (control) risk occur at a lower numerical value (due to the almost 4-times steeper slope of EFSA's transformed dose-response curve).

By altering the dose-response metric to "percentage of litters with 3 or more cases of PPL", EFSA's 2015 analysis also makes it (incorrectly) appear that PPL was absent in the control litters. There was PPL seen in the control animals, as would be expected biologically. The baseline rate of PPL is approximately 8% (see red hatched line in the figure above, calculated from Lang (1993)). The Springborn DRF study did have a low PPL rate of 2.1%, but it was not zero. The EFSA metric "zeroes out" PPL in control animals, suggesting that there is no PPL seen in the reproduction among the control animals. This further alters the dose-response, making it appear that there is no PPL seen in control animals. Finally, the intent of the BMD approach is the consideration of the entire dose-response relationship in characterizing the risk of the test item. By failing to include PPL events less than 3 per litter, these data are effectively "lost" from the analysis, minimizing the value of using a BMD approach.

In the Springborn DRF study (SLI, 2000a), out of eight control (unexposed) dams, one had 2 PPL cases,

two had 1 PPL case, and the remaining 5 litters had no PPL incidence. For the control animals, the EFSA analysis would suggest that there was no PPL in the controls, whereas there was 2.1% PPL among the controls in the DRF. When the DRF and both (F1 and F2) generations of the Springborn definitive study (SLI, 2000b) are considered (n=57 dams/litters) the rate of PPL (% per litter) among the controls was 5.6±1.7% (95% confidence limits). This central tendency value (and associated measure of variability) included 29 litters with no cases of PPL, 12 litters with 1 case of PPL, 13 litters with 2 cases of PPL, and 3 litters with 3 cases of PPL. The consideration of the test data in this way (on a per litter basis) is the most correct, scientifically, because the test item is applied to each dam individually. The dose is applied to the dams, so from a statistical perspective, the dams are the experimental unit, and their litters are true replicates. The EFSA 2015 analysis uses the treatments as experimental units, and is therefore incorrect, as are the BMDs derived therein.

Within these ranges of TRVs and considering the variability and uncertainty inherent in TRV derivation, the MOECC considers that the TRV of 11 µg/kg-bw/day is an appropriate and reasonable estimate for assessing oral Ni exposure and protecting against reproductive and developmental Ni toxicity.

Vale response: The TRV derivation already includes two 10-fold multiplicative uncertainty factors, resulting in a total uncertainty factor of 100. The selection of the point of departure must reflect the most appropriate interpretation of the experimental weight of evidence, including the use of historical data, without consideration of uncertainty factors. Uncertainty factors would then be applied independently of the statistical analysis to derive a conservative TRV.

TRV of 11 µg/kg-bw/day is also protective of effects on the male reproductive system for both adult males and toddlers

Several studies have provided evidence of an association between Ni exposure at low doses and the male reproductive system. EFSA (2015) used the potential toxicological effects on male fertility to support its selection of a POD of 0.28 mg/kg-bw/day for assessing post-implantation loss in rats. EFSA (2015) cited two studies conducted by Pandey et al. (1999, 2000) which indicated adverse effects of Ni on sperm (decreased sperm count and motility and an increase in abnormal sperm) and on accessory sexual organs (decreased weight of seminal vesicle and prostate gland) in mice at oral doses as low as 1.1 mg/kg-bw/day. While these studies were not considered adequate for the hazard characterization by EFSA (2015), a preliminary dose response analysis on sperm motility and sperm count conducted by EFSA (2015) estimated a BMD_{05} and $BMDL_{05}$ varying from 0.42 to 0.38 mg Ni/kg-bw/day for sperm motility, and from 0.62 to 0.46 mg Ni/kg-bw/day for sperm count.

Study limitations such as poor documentation and data inconsistencies and potential confounding effects of feed restriction, were cited in the CBRA by Stantec in their rationale for considering the evidence on the toxicity of Ni in the male reproductive tract and function. Even though these confounding factors cannot be ruled out, these studies provide supportive evidence on the adverse impact of Ni on the male reproductive system, particularly since these effects were observed at concentrations lower than the NOAEL of 5 mg/kg-bw/day for body and organ weight changes reported by Ambrose et al. (1976) and the NOEAL of 1.1 mg/kg-bw/day from the Springborn studies, and were used by EFSA to support the POD based on post-implantation loss (EFSA
2015).

Pandey et al. (1999) also observed an increase in pre- and post- implantation loss at 2.2 mg/kg- bw/day when only male mice were treated with Ni. This suggests that the reproductive and developmental effects reported in the Springborn (2000a,b) studies may not necessarily be limited to parturition (as suggested by NiPERA in a separate briefing to the MOECC provided on May 17, 2012 (Oller, 2012). In addition, in a reproductive study conducted by Toman et al. (2012), a time-dependent degradation of the seminiferous tubes of the testis was observed in Ni exposed mice. The effects were observed at 3, 6, 9, and 12 weeks in male mice treated at puberty with 2.5 mg/kg-bw/day Ni in feed (Ni spiked chow). The study by Toman et al. (2012) was considered by the MOECC to support the observations made by Pandey et al. (1999) of adverse effects of Ni on sperm and on accessory sexual organs in mice. In contrast, in the CBRA, Stantec suggests that restricted feed in this study was a potential confounding factor on the observations. Although the confounding effects of diet cannot be ruled out, the finding from this study that the intake of Ni caused serious damage on spermatogenesis and the developing testicular structure was considered by the MOECC as valuable information in understanding the overall toxicity of Ni.

Taking in consideration all the published evidence on this toxicological endpoint, the MOECC considered that a TRV of 11 µg/kg-bw/day based on developmental and reproductive effects also confers protection against Ni toxicity to the male reproductive system. Therefore, the MOECC concurs with the application of the TRV of 11 µg/kg-bw/day to the toddler stage to ensure that potential adverse impacts to the developing male reproductive system are included in this CBRA.

Vale response: From a reproductive/developmental toxicity perspective, the Springborn study (SLI, 2000b), which was conducted under GLP principles, found there to be no biologically meaningful statistically significant dose-response relationships, as indicated in the passage below, which are the final two paragraphs from Spingborn's study report summary.

Oral administration of the test article over the course of two generations at dosage levels up to 10.0 mg/kg/day had no effect on F0 or F1 survival, growth, mating behavior, fertility, gestation, parturition or lactation. No treatment-related mortality or clinical signs of toxicity were noted in the F0 or F1 rats, or their offspring, at any dosage level tested. F1 and F2 pup viability and growth were unaffected by test article treatment, and no toxicologically meaningful differences were noted among the groups with respect to estrous cycling, sperm parameters, copulation and fertility indices, precoital intervals, gestation lengths, gross necropsy findings, or the onset of sexual maturation in F1 rats. Slight but statistically significant reductions in absolute and/or relative liver weight were observed in F0 males at the 10.0 mg/kg/day level and F1 males at the 5.0 and 10.0 mg/kg/day levels. These differences were not regarded as toxicologically significant since the relative liver weight values were less than 10% different from the respective control values. Furthermore, histopathological evaluations did not reveal any test article-related changes in the liver, reproductive organs, or other tissues examined in this study.

In summary, oral administration of nickel sulfate hexahydrate to rats over the course of two generations did not produce indications of toxicity or adverse reproductive effects at dosage levels up to 10.0 mg/kg/day. A slight reduction in adult male liver weight was observed at the 10.0 mg/kg/day level in F0 males, and at the 5.0 and 10.0 mg/kg/day levels in F1 males. However, no treatment-related histopathological effects were observed in the liver or other tissues of the 10.0 mg/kg/day rats. Based on these results, 10.0 mg/kg/day is considered a No-Observed-Adverse-Effect Level (NOAEL) for oral administration of nickel sulfate hexahydrate over two generations in rats.

These two paragraphs from the 2-generation Springborn study (SLI, 2000b), a study conducted according to the principles of Good Laboratory Practice (GLP), indicate that there were no statistical differences in sperm parameters or other reproductive indicators at a NOAEL (of 10 mg/kg/day) for oral administration of nickel sulfate hexahydrate (NSHH) (or 2.2 mg Ni/kg/day as Ni) over two generations in rats. The Pandey studies are not without several issues and are generally considered to be of poor quality. The reference to MOE (2013) provided in the Ministry's references below is included in Annex 5.

3) ***Oral provocation of Ni dermatitis in humans has been measured at a dose of 12 µg/kg- bw; a TRV of lower than 12 µg/kg-bw/day (WHO 2007) is supported.***

The WHO (2007) used a TRV of 12 µg/kg-bw/day for Ni based on a human study by Nielsen (1999) that identified the oral provocation of dermatitis (see TRV "E" in MOECC Figure A1). This study included 20 Ni sensitized individuals who were exposed to Ni under fasting conditions after consuming a Ni reduced diet for 48 hours; 9 of the 20 individual's experiences a flare-up of dermatitis following a single dose of 12 µg/kg-bw of Ni sulphate administered in drinking water. Of these 9 individuals who developed symptoms, 3 experienced a severe reaction (2 individuals developed a maculopapular rash, and "baboon syndrome" was observed in another). The dose of 12 µg/kg-bw Ni in drinking water is considered by the WHO (2005) as an acute LOAEL in fasting subjects since adverse impacts were observed in 45% of the exposure individuals. No uncertainty factors (UF) were applied to this dose by the WHO (2005) because the test subjects represented a "highly sensitive population". Stantec also considered this TRV in the Port Colborne CBRA but only in the sensitivity analysis as they consider that it is overly protective for the general population.

However, other agencies determined that an UF may be warranted as adverse effects were observed after a single oral exposure to Ni. DEPA (2008) applied an UF of 7 to account for "sensitized" to "highly sensitized individuals". Although they provide no elaboration of the foundation of this UF, DEPA derived a TRV of 1.7 µg/kg-bw/day (see TRV "F" in MOECC Figure A1). Recently, EFSA (2015) relied on an analysis conducted by Jensen et al. (2006) and applied BMD modeling to the Jensen (2003) dermatitis data. The dose associated with a 10% adverse effect (BMD_{10}) was estimated to be 2.6 µg Ni/kg-bw with a lower 95th confidence limit ($BMDL_{10}$) of 1.1 µg Ni/kg-bw. Using the $BMDL_{10}$, EFSA considered the large inter-individual variability in the immune response that might not be covered by the limited number of individuals examined in the selected study and applied a margin of error of 10, resulting in an equivalent
TRV of 0.11 µg Ni/kg-bw /day (see TRV "G" in MOECC Figure A1).

However, as noted by EFSA (2015), it cannot be predicted that all sensitized individuals will actually develop adverse reactions nor what percentage eventually will develop such reactions at the estimated levels of Ni intake. Since the studies included a highly sensitive study group exposed under fasting conditions to Ni sulphate in lactose capsules, absorption is assumed to be considerably higher than it would be from food. These considerations were used by EFSA to conclude that the use of these studies would be conservative for characterizing acute risks.

Based on these considerations, the MOECC does not support using these lower TRVs of 0.11 µg Ni/kg-bw or 1.7 µg/kg-bw/day for evaluating chronic exposure risk for dermatitis in the Port Colborne CBRA. However, the analysis by DEPA (2008) and EFSA (2015) refutes the argument that a TRV of 12 µg/kg-bw/day is overly protective for the general population as postulated in the CBRA. Instead, the MOECC believes that using the TRV of 11 µg/kg-bw/day based on reproductive and development effects in rodents is appropriate for evaluating the oral exposure
of Ni in the Port Colborne CBRA but that the TRV of 11 µg/kg-bw/day may not be fully protective for Ni-sensitized individuals.

Vale Response: Vale rejects the use of the sensitization endpoint for RBSC development under the CBRA. The sensitization of humans towards Ni is largely due to the exposure to Ni present in jewelry and clothing fasteners (snaps and zippers) plated with Ni. This is a significant world-wide problem, and regulatory initiatives such as that of the EU's Jewelry Directive have begun to deal with this inappropriate use of Ni, (i.e. plated on jewelry, clothing, and similar items) which are expected to readily come into direct contact with skin. Vale fully supports the view that Ni is inappropriate for uses which would result in direct contact with skin. However, the Ni sensitization problem is a global social health phenomenon.

Vale believes that this issue would be better dealt-with directly by governing health bodies rather than trying to implicate the soil Ni contamination as a root cause of sensitization and (or) a cause of exacerbation of Ni-induced allergic contact dermatitis in Port Colborne residents. To date, Vale has no perception or understanding that the exacerbation of allergic contact dermatitis due to Ni in Port Colborne is different than anywhere else in Canada. The Community Health Assessment Study (CHAPS) conducted in parallel to the CBRA indicated that the rate of Ni allergy was similar in Port Colborne than elsewhere in Canada. Vale considers that Ni allergic contact dermatitis is a societal issue that has a much more complicated solution than declaring that Port Colborne residents should be concerned with "chronic exposure risk for dermatitis". Indeed, a TRV of 11-20 µg/kg-bw/day may

not be protective for individuals sensitized to Ni as a result of inappropriate uses such as Ni-plated jewelry. The Update Report addressed this endpoint but did not develop RBSCs for this endpoint for the reasons discussed above.

Since the CBRA 2014 Update Report was submitted, Haber et al. (2017) developed a TRV for protection of Ni-sensitized individuals from flare-up of dermatitis from acute exposure – 4 µg/kg/d – in addition to baseline Ni in food.

The TRV of 12 µg/kg-bw/day should be applied as an intake dose; not an uptake dose

As noted, Stantec used the 12 µg/kg-bw/day TRV in their sensitivity analysis to account for Ni dermatitis but in that analysis, they converted this intake dose TRV (i.e., how much Ni is ingested), to an absorbed dose TRV (i.e., how much of the ingested Ni is absorbed into the body). In order to do so, Stantec relied on a number of assumptions outlined by Oller (2012). However, the current risk assessment paradigm that is followed by MOECC, Health Canada, and the US EPA is to rely on a TRV based on intake doses as they are related to the environmental media that is being monitored or regulated. For example, a TRV based on drinking water can be directly applied to a measured water concentration, and no assumptions on absorption are required for regulatory purposes.

At present, there are a number of limitations to assessing Ni exposure based on conversion of an intake dose to an uptake dose as there is insufficient knowledge about Ni absorption (especially in the toddler), and about absorbed doses that are associated with the toxicological effects.
Currently, information on estimated Ni exposure based on absorption of Ni is limited to short term adult human studies or rodent studies. However, it is not clear how the toddler exposure can be estimated with any degree of confidence since there are data gaps in our understanding and questions as to how well the rat absorption data are predictive of absorption in humans. In addition, the California Environmental Protection Agency (CAL EPA) notes that the absorption rate of Ni in children may be several times higher than observed in adults (CAL EPA 2005). In light of these considerations, the conversion of the intake doses to uptake doses is not supported by the MOECC.

Vale Response: Data in this area is sparse. Vale agrees that bioavailability correction adjusting only for the exposure medium is an appropriate approach. See Annex 3 for further discussion.

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Appendix B: Background Dietary Exposure to Ni in Port Colborne

Overall Conclusions on Dietary Exposure:

The ministry does not support using the estimated Ni concentrations in garden produce and supermarket foods that were developed for evaluating dietary Ni exposure in this CBRA, despite the extensive work that was done by Vale in attempting to develop a Port Colborne specific estimate for this exposure pathway. Deficiencies in sampling of both garden produce and supermarket food significantly limit the interpretation of these results and the final CBRA estimates for the Port Colborne diet fall within the low range of the expected community exposure to Ni through the diet. Instead of the estimates proposed in this CBRA, the ministry recommends that the overall average estimate from Health Canada's Total Diet Survey's between 2000 and 2007 should be used instead. Supermarket exposure should be similar throughout Canada and given that the available data from the CBRA report clearly indicate that Ni is elevated in local garden produce (i.e., locally grown fruits and vegetables), dietary exposure to residents of Port Colborne should be higher than the Canadian average; not lower as indicated in the report.

The ministry recognises that dietary sources of Ni is a major contributor to the baseline or background Ni exposure and recent findings from CCME and other regulatory sources have determined that dietary exposure alone may approach or exceed the recommended total daily intake of Ni from all sources. However, the ministry also acknowledges that there is variability and uncertainty associated with these estimates. As such, dietary estimates based on larger sampling of food such as the Health Canada Total Diet Survey are considered to be more reliable than the relatively limited information provided in this report. The overall average Health Canada estimated dietary exposure of Ni in food is 183.4 µg Ni/day or 11.14 µg/kg-bw/day for the
toddler based on the 2000-2007 surveys (CCME 2015, Appendix 9). In contrast, the estimated dietary Ni exposure developed by Stantec for Zone B (the combined residential scenario) ranged from 150.9 to 169.7 µg Ni/day (or 9.1 to 10.3 µg/kg-bw/day) depending on how the garden produce data was used. These dietary estimates for Port Colborne are lower than the most recent Canadian estimate of exposure (CCME 2015), but within the low end of the year-to-year variation from the Health Canada Total Diet Survey (2000-2007).

The ministry's concerns with the dietary estimate used in the CBRA are primarily related to: (1) limitations in sampling design (a relatively small number of samples are available to characterize Ni concentrations in locally grown fruits and vegetables and the majority of available data is for soils with Ni concentrations less than 1,500 mg/kg) and (2) that the estimated contribution of Ni from the supermarket food basket is lower than predicted for the average Canadian consumer resulting in a lower total Ni dietary estimate for residents of Port Colborne than the Canadian average. Overall, the proposed Ni levels in locally grown garden produce combined with the estimated Ni levels for the supermarket food basket used in this CBRA is not adequate to represent community exposure to Ni from the diet.

Ideally, the total Ni dietary estimate should be re-assessed for the Port Colborne CBRA using the Health Canada Total Diet Survey Ni estimate for supermarket exposure and the contribution of Ni from local backyard produce. However, in absence of that reassessment, MOECC recommends that the Canadian average estimate of 11.14 µg/kg-bw/day developed by CCME, based on Health Canada Total Diet Survey (2000-2007) of total dietary intake, should be used for the toddler resident in the CBRA and in calculation of the RBSC.

While the CCME's (2015) total dietary estimate does not consider the contribution of Ni from local produce, MOECC considers it to be an upper bound estimate of the mean for the following reason: CCME calculated the average Ni concentrations in food by including non-detect samples at the method detection limit concentration instead of using ½ of the detection limit as was done in the CBRA and as recommended by the Country Foods Guidance of Health Canada (2010).

The ministry recognises that there is some uncertainty with this approach as it assumes that the contribution of Ni from local produce may be accounted for if the total dietary Ni exposure based on Health Canada Total Diet Survey (2000-2007) of total dietary intake is an upper bound estimate of the mean instead of the average estimate. That assumption may not be supported. As a result, MOECC recommends that proposed risk management measures recognize that Ni exposure from locally grown garden produce may be a concern and that measures to reduce this exposure pathway should be available (e.g., build raised garden beds and use clean topsoil for areas with elevated Ni concentrations in soil).

Vale Response: This issue of local dietary exposure would be a concern if the TRVs such as EFSA's 2015 2.8 µg/kg/d or the Danish EPA's 11 µg/kg/d were scientifically correct. However, they are not scientifically sound values and do not meet reasonable expectations for scientific scrutiny.

It must be recognized that the rats in the Springborn 2-generation reproductive toxicity study (SLI, 2000b) were fed Purina Rodent Chow , which contained 1.45 ± 0.16 µg Ni/g (95% C.I., n=4 samples analyzed for Vale), derived entirely from naturally sourced ingredients. A detailed discussion of baseline (background) dietary exposures of laboratory rats to Ni is provided in Dutton et al. (2019) and here again in Annex 2. The Springborn study gavage dosed animals with NSHH in water. These doses were in addition to the baseline dietary Ni exposure. There was no NSHH in the baseline dietary exposure, so it is true that the controls received zero nickel, but only in terms of NSHH. The controls actually received a baseline dose of Ni that had been naturally incorporated in plant- and animal-derived ingredients in the rat chow used in the study, as do Canadians in their everyday diets. Therefore, the point of departure (POD) taken from the Springborn study is on an "in addition to baseline exposure" basis. EFSA and other regulatory agencies have apparently been unaware of this distinction. The failure to apply Ni non-cancer TRVs on an "in addition to baseline dietary exposure" basis results in the apparent paradox whereby Canadian toddlers would appear to be 'at risk' due to Ni exposure solely from the consumption of a typical Canadian supermarket diet. This paradox is resolved when it is realized that TRVs developed using Springborn (SLI, 2000a,b) are incremental in nature and are to be applied in addition to baseline (or background) dietary exposures. Refer to Annex 2 for a detailed discussion concerning the appropriate application of such TRVs.

Limitations in Sampling Design

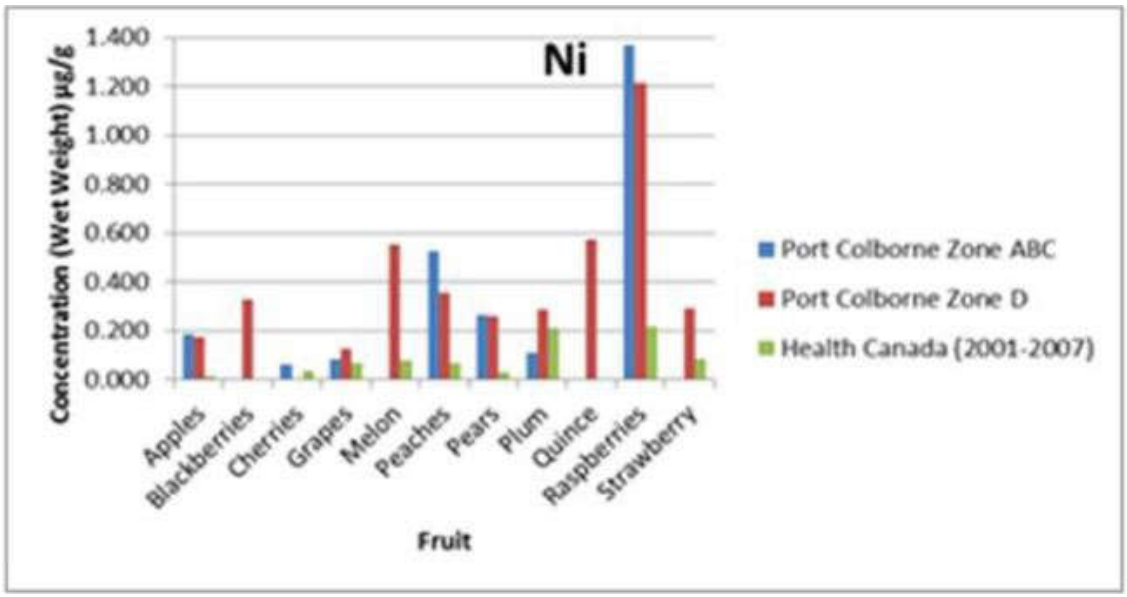
At first glance, the sample size for determining Ni in locally grown fruits and vegetables appears to be adequate in the CBRA report. For zone A, B, and C combined, a total of 30 fruits and 121 vegetables were collected. Similarly, Zone D had a total of 36 fruits and 102 vegetables collected. However, for individual fruits and vegetables, the sample size is often small (sometimes limited to one sample) and does not capture the range of Ni levels found in the garden soils examined. This should be viewed within the context to the larger multiyear composite samples collected by Health Canada in the Total Diet Study to characterize Ni levels in fruits and vegetables. The following table provides information on the number of times a fruit or vegetable was collected from the various zones

MOECC Table B1: Port Colborne Backyard Produce Samples

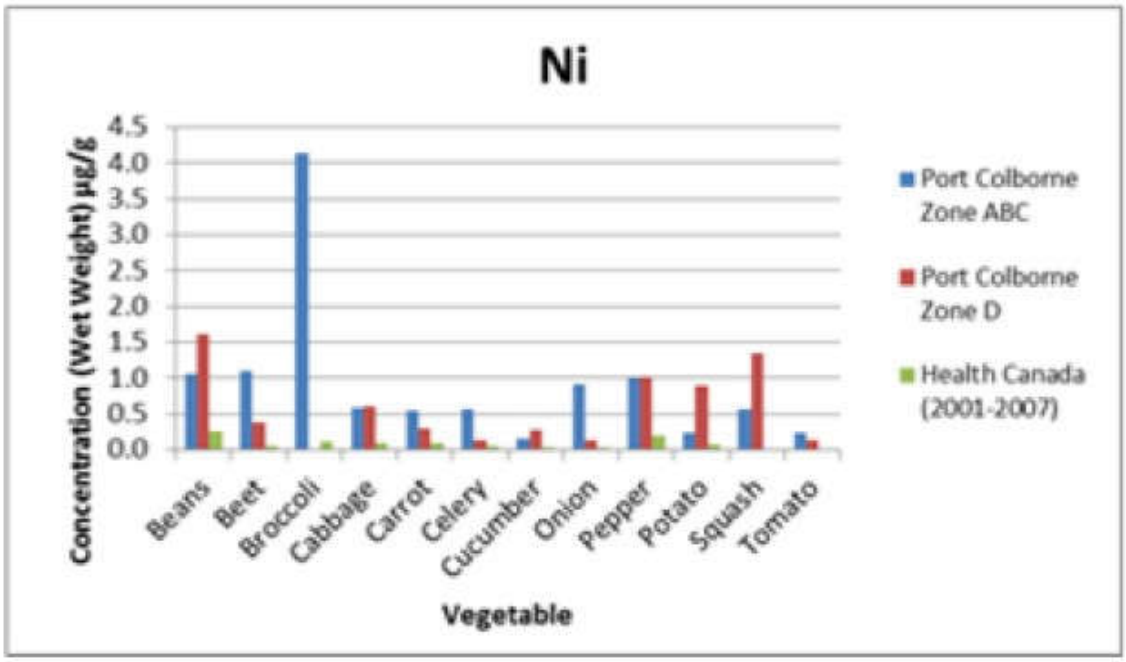
	Backyard Produce (Number of Samples Taken)	
	Fruit	**Vegetable**
Zone B (A, B, C)	30 (2, 1, 27)	121(0, 30, 91)
Zone D	36	102

It is clear from MOECC Table B1 that the majority of the samples for the combined zone A, B and C were determined from zone C (which doesn't include the most contaminated residential soil Ni levels). Overall, MOECC is concerned that the limited number of samples from the residential areas in Port Colborne significantly limits the interpretation of these results.

Despite the limitations in the available data for Ni concentrations in backyard garden produce, it is apparent that Ni concentrations are higher in fruits and vegetables from Port Colborne when compared to the average Canadian value. This is demonstrated in the CBRA report in Figure 3B.2 (Comparison of the Average Concentration in Backyard Fruits to the Average Concentration from the Health Canada Total Diet Study, 2001-2007) and Figure 3B.3 (Comparison of the average concentration in backyard vegetables to the average concentration from the Health Canada Total Diet Study, 2001-2007). These Figures are included below.



(Screen Grab Stantec 2014, Appendix 3B page 1-20)



(Screen Grab Stantec 2014, Appendix 3B page 1-21)

It is noteworthy that Ni levels are elevated even in samples collected from Zone D, an area with lower Ni soil contamination than found in Zone B. In addition, in some cases, there is very high uncertainty in the estimated Ni concentration in specific produce as the results are based on only one sample (e.g. the concentration for broccoli in Figure 3B-3 is based on a single sample). Another concern with the sampling design is that the majority of the data is for soils with Ni concentrations less than 1,500 mg/kg. No data is available for Ni levels in local garden produce when Ni soil concentrations exceed 6,680 mg/kg. According to the CBRA report (HHRA 2007), soil concentrations are a poor predictor of produce concentration; however, some relationships between soil Ni concentration and Ni concentrations in fruit (Peaches, Plums, and Strawberries) and vegetables (leafy vegetables, rhubarb) were identified in the CBRA report. A positive correlation of higher Ni in plants at higher soil Ni concentrations would be expected based on the results of the Crops ERA. While the backyard garden sampling was designed to represent community exposure, the available data does not reflect the upper end of expected soil Ni levels that can occur in residential gardens in Port Colborne (See MOECC Table B2 below). In addition, there is no information on the potential exposure to Ni from locally grown garden produce at the soil concentrations recommended in the CBRA report at the RBSCs (i.e., 48,000 mg/kg Ni in Zone B). Therefore, in absence of additional sampling, caution is warranted in using this information as part of developing the RBSC and in applying the recommended RBSC (that has not considered the potential for backyard garden produce grown in soil conditions at the RBSC) to contribute to the total dietary exposure.

MOECC Table B2: Port Colborne Garden Soil Ni Concentrations

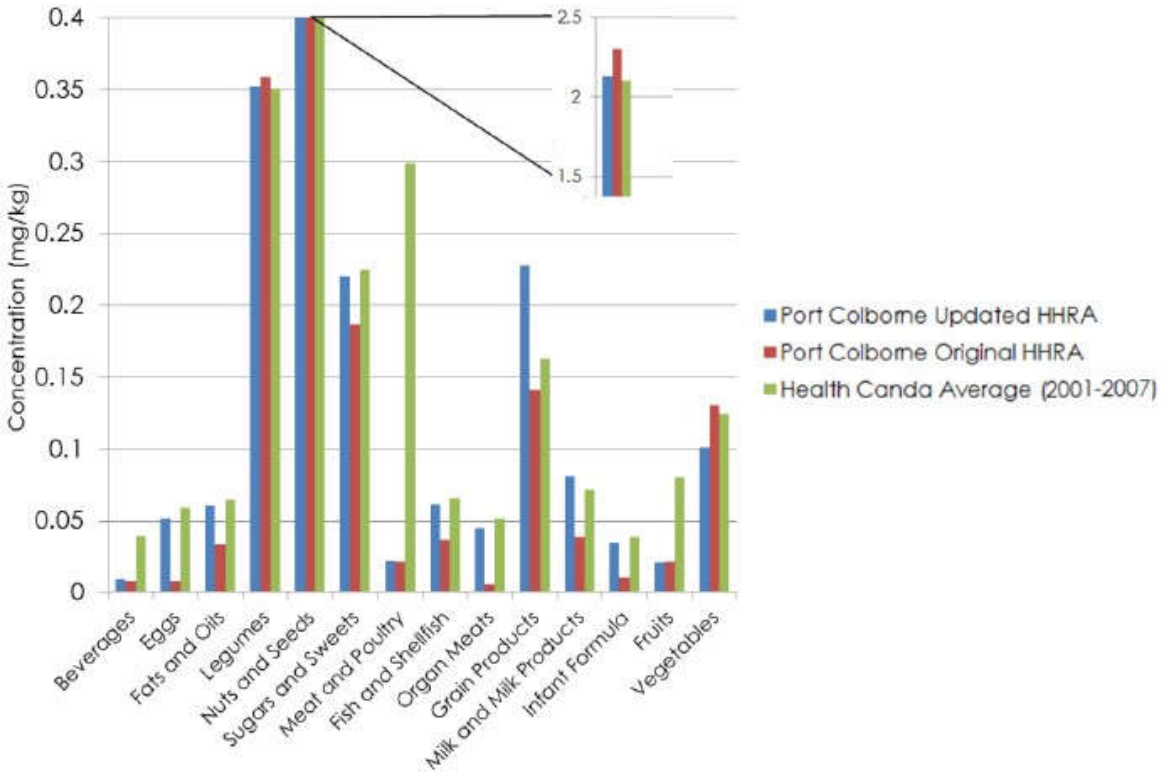
	Co-localized Garden Produce Soil Ni Concentrations			
Zone	**Average (mg/kg)**	**75th Percentile (mg/kg)**	**95th Percentile (mg/kg)**	**Maximum (mg/kg)**
B (ABC combined)	705	845	1552	6680
D	353	380	1450	2720

Vale Response: Comment received.

Estimated Contribution of Ni from the Supermarket Food Basket

For the supermarket exposure, the revised estimate developed by Stantec for Ni levels in various food products incorporates Port Colborne data supplemented with the Canadian data. This was done by Stantec using the following protocol: (1) for food categories with less than 10 samples, food concentrations were based on the average of the Port Colborne study but supplemented with the Canadian yearly averages (developed from a total of 8 data sets between 2001 and 2007) and (2) for food categories with 10 or more samples, concentrations food concentrations were estimated based on the higher of the upper confidence level of the (geometric) mean and the 75th percentile from the Port Colborne data only. As demonstrated in the CBRA report in Figure 3B.7 (Concentrations of Nickel in Supermarket Food), Ni concentrations used in the CBRA are generally similar to the Canadian average (2001-2007). However, notable exceptions are apparent where lower Ni concentrations are observed for the Port Colborne estimate for beverages, meat and poultry, and fruits (Figure 3B.7 provided below). For these food categories, it is unclear why the Port Colborne data should be lower than the Canadian average and raises questions regarding the adequacy of this Port Colborne specific Supermarket data to properly represent the community supermarket diet. It is noteworthy that consistent with the findings from the Crops ERA, higher Ni concentrations were observed for the Port Colborne estimate for the grain products food. The food categories beverages and meat and poultry are discussed in more detail below.

Figure 3B.7: Concentrations of Nickel in Supermarket Food



(Screen Grab Stantec 2014, Appendix 3B pp 1-29)

For the beverages food category, Ni concentrations are estimated to be 5 times lower in the CBRA than the Canadian average (HC Total Diet Study, 2001-2007). The discrepancy for this difference was not identified. However, the lower Ni content in this

category reported for Port Colborne is similar to estimates reported by the US FDA and the UK. While a total of 11 samples were collected (see Table 3B.7 of CBRA report, Food Categories and Sample Sizes used in the Port Colborne Food Basket Study), MOECC believes this food category should be treated as if it had less than 10 samples and that the data should be combined with the Canadian yearly average for non-alcoholic beverages. This is because the Port Colborne estimate includes inappropriate beverages for a toddler such as white wine, whiskey, coffee, tea, beer, and caffeinated cola drinks ((see Table E.2-1 Supermarket Food Results (Beverages) - Port Colborne Determination of Gravimetric Metal Concentrations Port Colborne CBRA June-August, 2002 (Volume V - Appendix 19, Local Supermarket Food Basket 2007)). These beverages samples should not be used to represent a toddler's intake for the beverage food category.

For the Meat and Poultry food category, the estimate is based on 22 samples (Table 3B.7 Food Categories and Sample Sizes used in the Port Colborne Food Basket Study). The estimated Ni in this food category is substantially lower than the average Canadian (2001-2007) estimate. The CBRA report accounts for this discrepancy by noting that special control for Ni during sample preparation and cooking was done (including the avoidance of Ni containing utensils and pots), to avoid any contribution of Ni from sample preparation. This was done because an earlier Canadian Total Diet Survey (Dabeka 1995), observed that new stainless steel cookware contributed to the Ni content of food. This finding was supported by a limited study undertaken by Jacques Whitford 2007 (Volume V, Appendix 19, Attachment D, Cooked Food Screening Study Report) that reported no significant contributions of Ni occurred due to cooking in a well-used stainless steel pan in comparison to a ceramic pan. As mentioned in the CBRA report (page 1.25 of Appendix 3B, Changes in Input Assumptions and Data), Health Canada did not process food with specific control for nickel, that cookware is typically reused from year to year, and that Health Canada does not keep track of when specific cooking items are replaced with new ones. Therefore, Stantec concluded that "it is possible that the elevated concentrations of nickel reported in meat and poultry from the Health TDS (2001-2007) are due to the release of artificial nickel from the use of new stainless steel cookware". MOECC does not dispute that Ni may be released into the meats and poultry as part of food preparation and cooking. However, the Health Canada Total Diet Study contains appropriate and valid data as it uses food preparation and cooking methods that are reflective of typical cooking methods. It is unreasonable to assume that local residents in Port Colborne would not cook with stainless steel cookware and that they would not be replaced from time to time. In addition, given that Health Canada's data is based on a much larger multiyear sampling (2000-2007) and that they re-used cookware, any release of Ni associated with brand new stainless steel cookware would not be expected to repeatedly occur. It is also noted that the Health Canada Total Diet Study has recently been used by CCME (2015) to estimate total Ni dietary intake in developing the most recent Canadian Soil Quality Guideline.

Based on these examples, and given the limited Port Colborne sampling, MOECC recommends that for estimating the supermarket food basket, the Health Canada estimate should be used or that all food categories should be combined with the Canadian yearly averages. It is anticipated that this would result in a higher estimate of supermarket dietary exposure for the average Port Colborne toddler used in the CBRA.

Note: some discrepancies in reported values were noted between the written text in the updated CBRA report (2014) and the model provided to the ministry by Stantec. In order to facilitate the MOECC's review of the CBRA, the model values are reported.

Vale Response: Comment received. Given that the appropriate application of any TRV based on the Springborn (SLI, 2000a,b) data is in addition to baseline (or background) dietary exposures, the Port Colborne-specific incremental contribution of backyard garden produce to baseline

dietary exposures is an important consideration.

***References*:**

Canadian Council of Minister of the Environment (CCME), 2015. Scientific Supporting Document for Canadian Soil Quality Guidelines for Nickel: Environmental and Human Health. CCME 2015.

Dabeka RW and McKenzie AD (1995) Survey of lead, cadmium, fluoride, nickel, and cobalt in food composites and estimation of dietary intakes of these elements by Canadians in 1986-1988. J. of AOAC International, 78(4), 897-909.

Health Canada, 2010. Federal Contaminated Site Risk Assessment in Canada: Supplemental Guidance on Human Health Risk Assessment for Country Foods ($HHRA_{foods}$). Ottawa. H128-1/11-641E-PDF.

Health Canada, 2000-2007. Average Concentrations (ng/g) of trace elements in foods for Total Diet Study in 2000-2007. Health Canada. Available online at: http://www.hc-sc.gc.ca/fn-an/surveill/total-diet/concentration/index-eng.php

References used in Vale's Response:

Dutton, M.D., L. Vasiluk, F. Ford, M. Bellantino Perco, S.R. Taylor, K. Lopez, G.T. Bolger, Y. Gopalapillai, and B. Hale. 2019. Towards an exposure narrative for metals and arsenic in historically contaminated Ni refinery soils: Relationships between speciation, bioavailability, and bioaccessibility. Sci. Tot. Environ. 686: 805-818. https://doi.org/10.1016/j.scitotenv.2019.05.164.

SLI 2000a. Springborn Laboratory Inc. A One-Generation Reproduction Range-Finding Study in Rats with Nickel Sulfate Hexahydrate. Final Report. Springborn Laboratory, Inc. Study No. 3472.3. Submitted to: NiPERA, Inc., Durham, North Carolina, USA.

SLI 2000b. Springborn Laboratory Inc.An Oral (Gavage) Two-Generation Reproduction Toxicity Study in Sprague- Dawley Rats with Nickel Sulfate Hexahydrate. Final Report. Springborn Laboratory, Inc. Study No. 3472.4. Submitted to: NiPERA, Inc., Durham, North Carolina, USA.

Appendix C: Bioavailability/Bioaccessibility of Ni in Port Colborne Soils to People via Ingestion Route

Overall Conclusions on Bioaccessibility:

The ministry supports the general argument that not all of the Ni in soil is biologically available. That is, if a person consumes soil containing Ni, not all the Ni would be available for absorption from the soil in the gastrointestinal tract (i.e., bioaccessible) and the resulting absorption of Ni into the bloodstream would be less than 100% (i.e., bioavailable). However, the ministry does not support the approach used in the risk assessment to estimate the bioaccessibility of Ni. Specifically, the ministry believes that the estimates are too low and, for the purpose of this risk assessment, underestimate Ni exposure from soil and the risk resulting from incidental ingestion. A summary of the key issues are provided below followed by a detailed discussion.

Summary of Key Issues:

1. ***MOECC does not support Ni bioavailability estimates from in-vivo studies with rats***

Laboratory studies on rats were conducted for this CBRA to estimate the amount of Ni that is absorbed from ingestion of Ni in Port Colborne soil. This *in-vivo* estimate is not supported by the ministry for the following reasons:

- Bioavailability studies using Ni: There is no approved method for estimating absorption of Ni from *in-vivo* studies. The approach followed for the other COCs in the risk assessment was based on *in-vitro* bioaccessibility studies. This information is also available for Ni and is more reliable for use in the risk assessment.
- Species tested: The bioavailability studies were conducted using adult rats.
    - Rats are not an appropriate species for estimating Ni absorption from the gastrointestinal tract because they have a different gut physiology from humans and do not reflect human absorption; and
    - The adult rat is not relevant for estimating bioavailability in a human toddler (which has the highest estimated exposure to Ni in soil through incidental ingestion).
- Experimental conditions: A single dose was used in the experiment.
    - Depending on the soil type, the bioavailability of Ni in soil may be greater at lower soil concentrations. Since mainly high soil Ni concentration were evaluated in these experiment, the estimated bioavailability may not be applicable to some of the Ni soil concentrations in Port Colborne that are appropriate for the residential community; and
    - The single dose tested was not sufficient to achieve steady state conditions as expected under chronic conditions thus limiting the interpretation of the study.

2. **MOECC does support using bioaccessibility estimates from *in-vitro* studies**

New bioaccessibility data has been provided and has contributed greatly to the understanding of bioaccessibility for the various soil types and has filled significant data gaps identified previously by MOECC.

The ministry reviewed the Ni bioaccessibility estimates made for the three soil types: fill, clay and organic soil; and recalculated the Ni bioaccessibility using all of the fill data (including the

2002 Exponent data for the fill soil that was omitted by Stantec) and using the 95th upper confidence limit of the mean (95th UCLM) rather than the mean. The 95th UCLM should be used in the risk assessment as a reasonably conservative and supportable estimate of the fraction of Ni in soil that is soluble in the human gastrointestinal environment and available for absorption. Based on the ministry's recalculations, the estimated bioaccessibility of Ni in soil is now much higher than those values used in the CBRA. Estimated Ni bioaccessibility that is supported by the MOECC is provided below (MOECC Table C1) along with a comparison to the values referenced in the CBRA sensitivity analysis. Additional discussion of the bioaccessibility values supported by the MOECC is provided in the detailed comment section below.

MOECC Table C1: Comparison of Stantec/Vale Bioaccessibility Calculations to MOECC Recalculations

Soil Type	Stantec Calculations (Mean) Ni Bioaccessibility (%)	MOECC Calculations (95th UCLM) Ni Bioaccessibility (%)
Fill	*8.7 (without 2002 Exponent data)	21 (with 2002 Exponent data)
Clay	9.4	15
Organic	22	32

* used in the sensitivity analysis by Stantec (note: 5.8% bioavailability was used in the CBRA)

Detailed Comments on Bioavailability and Bioaccessibility

1. ***Inappropriate Reliance on in-vivo Data Derived from Studies using an Adult Rat to Estimate the Relative Oral Bioavailability in Human Toddlers***

MOECC has significant concerns with the reliance on *in-vivo* data derived from studies using an adult rat to estimate the Relative Oral Bioavailability (ROB) for human toddlers. Specifically these concerns are:

- Inappropriate use of the rat model to investigate soil oral Ni bioavailability.
- Limitations in the *in-vivo* study design and context to existing literature on Port Colborne soil bioavailability.
- Limitation in the extrapolation of bioavailability information to predict absorption of Ni in toddlers.
- Inability to develop a ROB for toddlers because critical information is missing from the key studies used for the oral Ni TRV.

The inappropriate use of the rat model together with the limitations in the bioavailability testing preclude the use of this *in-vivo* bioavailability information in the determination of the ROB for use in the Port Colborne CBRA.

Vale Response: Responses to these individual bullet points are interleaved in each section.

Inappropriate use of the in-vivo rat model to investigate Ni soil oral bioavailability.

In general, the rat model is an inappropriate model to investigate the soil oral bioavailability of Ni and is not recommended by other regulatory agencies. This is supported by Health Canada (2010), which notes that "…laboratory rat species appear to be inappropriate for *in-vivo* investigations of oral bioavailability from soil". Physiologically, the rat gut is different than

humans, in that it has a two compartment stomach (including a fore-stomach) rather than a one compartment stomach. As a nocturnal feeder, the fore-stomach functions to store food for later digestion. Consequently the rat stomach does not reach a low pH of 1 -2 that is typical in humans under fasting conditions and associated with increased Ni uptake. In humans under experimental conditions, there is a decrease in Ni absorption when Ni is taken with food. Experimentally, a low pH has been demonstrated to liberate more Ni from Port Colborne soils thus increasing the available Ni for absorption. As a consequence, the rat model would not liberate as much Ni from soil as would be expected in humans under fasting conditions and cannot be relied on for estimating a health-protective soil Ni bioavailability estimate.

In soil bioavailability testing, the accepted *in-vivo* models rely on testing done with a juvenile pig (as used in the IEUBK US EPA model for Pb, US EPA 2002). The juvenile swine gut is more physiologically comparable to that of the human toddler. In the revised report, Stantec refers to the use of the rat *in-vivo* data as being the "gold standard" (page 3.77). This statement is not supportable. The "gold standard" would be a chronic, multiple exposure *in-vivo* study with juvenile pigs.

Vale Response: Health Canada (2010) also made the following statement regarding the use of rats for in vivo bioavailability estimation (p. 52, section 4.7.3.1 of Health Canada (2010) [Federal Contaminated Site Risk Assessment in Canada, Part V: Guidance on Human Health Detailed Quantitative Risk Assessment for Chemicals (DQRAChem)].

> ***It should be noted, however, that laboratory rat species appear to be inappropriate for in vivo investigations of oral bioavailability from soil. A review of published studies pertaining to arsenic (As), cadmium (Cd), and lead (Pb) concluded that bioavailability of these soil-borne contaminants in rats was consistently low relative to other mammalian species, including humans (JWEL, 2005).***

Health Canada's citation of JWEL (2005) refers to the report entitled "Ingestion bioavailability of Arsenic, Lead, and Cadmium in Human Health Risk Assessments: Critical Review and Recommendations. Prepared for Health Canada Environmental Health Assessment Services, Safe Environments Program. Project No. N050604." The JWEL (2005) report, which is available online (http://www.bioavailabilityresearch.ca/Health%20Canada%20Bioavailability.final.pdf) reviewed several studies and purported to show that arsenic bioavailability in rats was the lowest among several different animal species. The Health Canada (2010) and JWEL (2005) reports raise more questions to Vale than they provide answers, and they certainly do not unequivocally demonstrate that a rat model is inappropriate for studying bioavailability. The studies that used rats for estimating bioavailability did not uniformly indicate lower bioavailability estimates, and the two papers by Ng et al. (Ng et al. 1998 and Ng et al. 2003) cited by JWEL (2005) reported arsenic bioavailability differently. Secondly, the values reported by JWEL (2005) in the report to Health Canada do not appear to reflect the information present in the original papers by Ng et al. Vale will not critique the JWEL (2005) report in detail here, but considers the report to be flawed. The studies reviewed by JWEL (2005) covered a wide range of methodological differences. The differences among the speciation of As, Pb, and Cd compounds presented within each of these different studies makes it difficult (if not impossible) to compare the results in any meaningful way. However, it is of interest to Vale that the JWEL (2005) report clearly recommends that for Ni, at least, a rat model should be used for bioavailability studies for Ni in soil, since the toxicity study upon which the TRV is based is also a rat model. The following passage is taken from p. 19 of JWEL (2005).

In the case where oral toxicity reference values for use in human health risk assessment have been derived from a specific test species, then it would be most appropriate to use that test species in the development of oral bioavailability of contaminants from soil. For example, the United States Environmental Protection Agency (US EPA) oral reference dose (RfD) used in the toxicity assessment of oral dose of nickel from soils of 20 µg/kg-d, was derived from the no observed adverse effect level (NOAEL) from a feeding study of rats with nickel dosed food (US EPA, 1987). The RfD is used as an administered dose and thus the oral bioavailability is accounted for in the administered dose. Therefore, subsequent bioavailability studies of nickel from soil should employ a similar rat model so that administered doses could be compared.

This comment was not carried forward by Health Canada, but makes perfect sense. In cases where TRVs have been derived from rat studies, it makes sense to use a rat model to ascertain site-specific bioavailability in human health risk assessments which rely on a TRV derived from a rat study (with uncertainty factors of 100 applied to the point of departure). The consideration of site-specific bioavailability in rats is a logical approach in cases where a TRV has been derived from a rat study.

Limitation in the extrapolation of bioavailability information to predict absorption of Ni in toddlers.

There is an inherent limited ability to use animal models to make predictions on the absorption of Ni in the toddler. Even with available information in humans there is variability in absorption of Ni between the adult versus the toddler. This is highlighted by Cal EPA (2005) that considers Ni absorption in the toddler to be generally 10 times greater than the adult. In addition, Cal EPA 2005, which developed a child specific Ni TRV (chRD) do not recommend applying an adjustment for bioavailability or bioaccessibility when conducting an exposure assessment because of uncertainties associated with predicting update in toddlers (See also MOE 2011, HHRA review comment #18). Cal EPA recommendation supports a prudent approach when considering the ROB for the assessment of the toddler to ensure that Ni exposure from soil is not underestimated.

Compounding this issue is the fact that the rat model used by the proponent is an adult that does not represent a toddler stage. In rats, the juvenile stage is considered less than 21 days old. In spite of these limitations, the *in-vivo* information is considered further by the ministry as the Ni oral TRV used in the CBRA was determined using a rat model and additional discussion is warranted.

Vale Response: Vale agrees with the Ministry that animal models have a limited ability to predict the absorption of substances ingested orally by humans. Nevertheless, the rat is the most heavily studied and common mammalian model for use in clinical studies of pharmaceuticals and other substances. Both key studies used as the basis for TRVs (Ambrose et al. 1976 and SLI, 2000a,b) used rats. It seemed obvious to Vale to use a rat model to conduct further studies to supplement the findings of the original rat bioavailability study conducted in the CBRA. The use of other animal models (juvenile swine or primates) is fraught with difficulties and their value is overstated. Rat studies represent a logical approach for understanding nickel risk.

Limitations in the in-vivo study design and context to existing literature on Port Colborne soil bioavailability.

Even though the rat was used in the determination of the Ni TRVs, there are general limitations in the study design (in addition to the above noted limitations to the rat model) that do not support the use of the *in-vivo* information in the ROB estimate. The *in-vivo* experimental design included the dosing of male Sprague-Dawley rats with a single gavage dose of $NiSO_4.6H_2O$ or with soil containing Ni. The absorption of the control test substance nickel sulfate has been reported as high as 39% (Vasiluk et al., 2011). This absolute bioavailability is substantially higher than what is expected under chronic conditions. Under chronic conditions, the absolute bioavailability is expected to be much lower in the low percent range (e.g., 5%) under steady state conditions. As steady state conditions were not reached in the experiment conducted for this CBRA, this raises concerns about the representativeness and utility of a single dose scenario to provide an estimate of the relative absorption between soil and the control test substance.

In these experiments, in order to detect absorbed Ni in urine, the rats received a large quantity of soil. It is expected that this will disproportionally affect the stomach pH, essentially mimicking greater feed state, in comparison to the control test substance dosing. It is also important to note that specific details on dosing were not available for the MOECC review (Vale 2012) and therefore our comments are based on the assumption that there are no concerns with that data.

An additional degree of uncertainty is raised in the ROB estimates (ranging from 5.8% to 22%) used in the revised CBRA report in comparison to a higher 56% reported in Vasiluk et al., (2011) for a Port Colborne soil sample (based on an absolute bioavailability of 22 ± 12% in comparison to the 39% absolute bioavailability of the control test substance ($NiSO_4.6H_2O$)). A direct comparison from this study to the Port Colborne CBRA cannot be made as a particle fraction of the soil sample tested (particle size ranged between 150-250 µm at a soil concentration of 1720 mg/kg) differs from the standard testing procedure and the vehicle for the control test substance dosing was different.

Vale Response: The Vasiluk et al. (2011) value cited by the Ministry is a 24-hour estimate based on the partially complete fecal mass balancing of the applied dose. The value reported by Vasiluk et al. (2011) should therefore be considered to be a lower-tier data source. Dutton et al. (2019) have provided context for this result that was not available when the Ministry reviewed the Update Report.

The single dose of NSHH provides a "clean" estimate of oral bioavailability with no concern over carry-over from dosing in previous days. There is no inherent reason to think that bioavailability is different after one or many days of exposure; there would just be different technical considerations as to how to measure it after repeated doses. Refer to Annex 3 for an in-depth discussion concerning the interpretation of nickel bioavailability in Port Colborne.

Inability to develop a ROB for toddlers because critical information is missing from the key studies used for the oral Ni TRV.

The absolute bioavailability or absorption of Ni was not determined in the rat study by Springborn 2001 (supporting the TRV of 11 µg/kg-bw/day) or the human study by Neilson et al., 1999 (supporting the TRV of 12 µg/kg-bw/day). This limits the ability to develop relative oral bioavailability estimates. While a ROB based on literature values could be estimated, it would be of limited value as most of the available information is confined to the adult and not the toddler

receptor.

Vale Response: The in vivo studies conducted by Vale included two "mini-studies" (Dutton et al., 2019). The mini-studies mimicked the bioavailability of NSHH under conditions of the Springborn study and approximating that of the Ambrose study (the two studies mostly commonly used as the basis for TRVs). The term "approximated" is used because in the Ambrose study, exposed rats were allowed to feed freely (ad libitum) on NSHH added to rat chow, but in Mini-study #2 (Dutton et al., 2019) the Ni-spiked rat chow was dosed to rats by gavage to ensure accurate dosing, which could not be obtained from the original Ambrose study. The correction for oral bioavailability was achieved by comparing bioavailability from the "Springborn" mini-study with the "Ambrose" mini-study and applying this estimate of relative oral bioavailability to the human receptor for which risk is being assessed. This follows from the Ministry's own direction to Vale for both the Sudbury Soils Study and the CBRA in its memo entitled "Port Colborne CBRA HHRA – MOE comments on May 2005 draft (as presented to the proponent on September 6, 2007)"

2. Inappropriate Screening and Analysis of in-vitro Bioaccessibility Data

Bioaccessibility can be determined in a test tube (referred to as an *in-vitro* assay) under standardized laboratory conditions. The procedure consists of a 2-step process that mimics conditions in the stomach (phase one) and the intestine (phase two). Although, an established method for determining Ni bioaccessibility in soil does not currently exist, the methods used in the CBRA to determine bioaccessibility in Port Colborne soils are similar to the method used and accepted by the US EPA (2007) for lead (Pb), arsenic (As) and some other metals. For Ni, the first phase of the process, that mimics conditions in the stomach (under acidic or low pH conditions) is the phase used in the assessment of Ni bioaccessibility.

In this CBRA update report, Stantec considered the *in-vitro* bioaccessibility data for Ni only in their sensitivity analysis. However, *in-vitro* bioaccessibility data was used in the main analysis for the other COC's (Cu, As and Co). The estimated ROB values for Ni in soil have been revised for each of the 3 soil types (fill, clay, and organic) in this CBRA update report but rely only on new data from Vale 2012 and previous data from JWL 2002. The *in-vitro* data developed by Exponent 2002 and used by the MOE in the Rodney Street Risk Assessment (2002) was not used.

The bioaccessibility values presented by Stantec in the updated CBRA report are generally higher than those in the earlier version of the CBRA, and now are specific to each soil type based on the new information from Vale 2012. For Ni, the revised *in-vitro* bioaccessibility values are 8.7% for fill soil, 9.4% for clay soil, and 22% for organic soil. These values are all higher than the previous version where Ni ROB was estimated at 4% for all 3 soil types.

MOECC reanalyzed the *in-vitro* bioaccessibility data for all three soil types using all of the bioaccessibility data (Exponent 2002, JWL, 2002 and Vale 2012). This re-analysis is presented below for each of the soil types.

Fill Soil Type: Inappropriate Analysis of in-vitro Bioaccessibility Data

Overall, a small number of soil sampling locations were used to represent the variability of Ni bioaccessibility in the Fill soil type. While the revised CBRA report suggests a sample size of 6, only 2 soil locations were tested (TP17 and TP9). The variability in the soil matrix has not been

sufficiently addressed by using repeated sampling from the TP9 location (5 of the 6 soil samples used to determine the bioaccessibility estimate were from TP9 (see Table 3E-3). Although these soil samples cover a large range of Ni soil concentrations (from about 8,800 to 17,500 mg/kg), the bioaccessibility estimates for TP9 are relatively stable at 7.0 ± 0.8% (mean ± standard deviation). This can be compared to the one measurement at TP17 (soil Ni = 3,265 mg/kg), where the Ni bioaccessibility estimate is much higher at 17.0%. Comparing the results from TP9 and TP17 suggests that the Ni concentration in the soil and/or the soil sampling location has a strong influence on Ni bioaccessibility. The data was re-plotted by sample location to reflect the influence of sample location and soil conditions on Ni bioaccessibility (MOECC Figure C1).

Vale Response: Vale recognizes that these samples were from a small number of test pits. The samples were archived and had been characterized in the CBRA and were available to conduct a bioavailability study. Despite these issues, it is the underlying speciation that determines the bioavailability, so there is value to this research.

Fill Soil Type: Inappropriate Screening of in-vitro Bioaccessibility Data

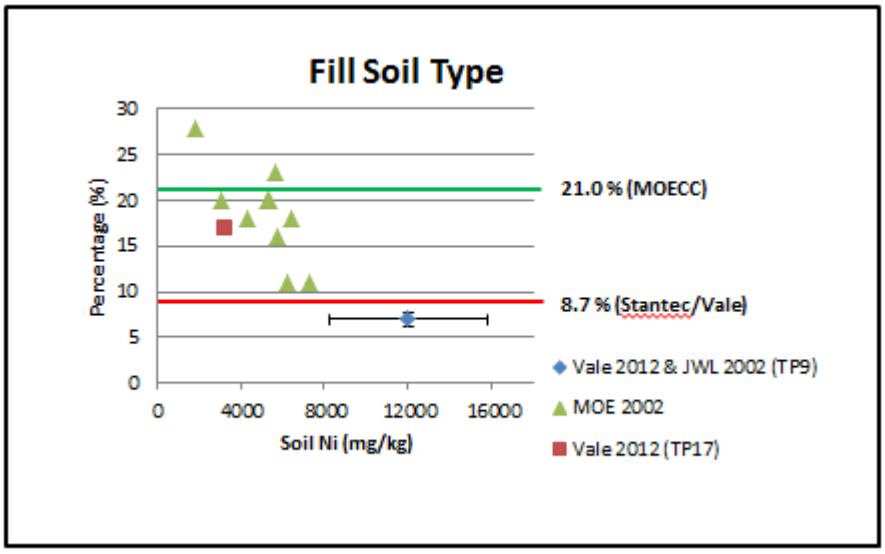
The original bioaccessibility information determined by Exponent (2002) should also have been used to estimate the bioaccessibility for the Fill soil type. This Exponent data was not used in the revised CBRA report by Stantec despite being used in previous version of the CBRA primarily due to concerns with potential interference from the glycine buffer used in the Exponent (2002) testing procedure. However, the effect of glycine buffer (isoelectric point pH 6) is limited to potential interference in the second phase (phase two - intestinal) bioaccessibility estimate; not the first phase (phase one - stomach) bioaccessibility estimate. MOECC believes the Exponent data is valid and should be used to determine Ni bioaccessibility since the phase one data is not compromised by the additional of the glycine buffer.

Another concern Stantec had with the Exponent data was that there was higher average bioaccessibility estimates in the Exponent (2002) samples which Stantec/Vale attribute to the presence of organic soils. As noted in the revised CBRA report, organic soils are predicted to have higher bioaccessibility than Fill or Clay soil samples. MOECC believes that the Exponent (2002) samples are representative of the Rodney Street community, which has been characterized using the general term of "Fill" to reflect the variable nature of the soil type and to reflect that it is neither organic or clay soil types. Together, the Exponent (2002) samples are considered by the MOECC to be valid phase one (stomach) bioaccessibility estimates that represent 10 sample locations within the Rodney street community at expected soil Ni levels (all less than 8,000 mg/kg) and therefore, were considered in the re-analysis of the Fill soil type.

Fill Soil Type: Re-analysis of the ROB

There appears to be a relationship between Ni bioaccessibility and soil Ni concentration where Ni bioaccessibility is higher at lower soil Ni levels (MOECC Figure C1). This relationship can be statistically determined with high confidence (see Section 3 below). However, MOECC believes that a reasonable conservative (i.e., erring on the side of caution) estimate is to use the 95% UCLM (an upper estimate of central tendency). This is consistent with the MOECC practice for all risk assessments. Using all of the bioaccessibility data (including the data from Exponent, 2002) results in a 95% UCLM of 21% for fill soils (see MOECC Figure C1 and Table C2 below). Note: this recommended bioaccessibility estimate captures the range of bioaccessibility for soils with Ni concentrations <8,000 mg/kg (which range from 11 to 28%).

MOECC Figure C1



MOECC Table C2: The following data was used to determine the Fill soil bioaccessibility estimate:

		CBRA Report (2014)		Re-analysis (MOECC)	
In-vitro Experiment	**Sample Location**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**
Vale (2012)	TP17	3265	17	3265	17
Vale(2012)	TP9	13848	6.7	12007 ± 3752	7.0 ± 0.8
Vale(2012)	TP9	17420	7.7		
Vale(2012)	TP9	8680	7.8		
Vale (2012)	TP9	8489	5.8		
JWL (2002)	TP9	11600	6.9		
Exponent (2002)	1			7310	11
Exponent (2002)	2			1840	28
Exponent (2002)	3			5370	20
Exponent (2002)	4			6410	18
Exponent (2002)	5			5620	23
Exponent (2002)	6			5730	16
Exponent (2002)	7			6200	11
Exponent (2002)	8			5290	20
Exponent (2002)	9			3040	20

Exponent (2002)	10			4270	18	
			8.7		17.4	**Average (Mean)**
					21.0	**95th UCLM**
					28.0	**95th ile**

Summary Point Estimate of Bioaccessibility for Fill Soil Type

For the HHRA, the 95th UCLM of the Fill soil type data at 21.0% bioaccessibility is supported as a CTE estimate. For the sensitivity analysis, the 95th percentile at 28.0% bioaccessibility is supported as a RME estimate.

Vale Response: As mentioned in the previous response, the Ministry's data overestimate (provide a conservative estimate of bioaccessibility.

Clay Soil Type: Inappropriate Analysis of in-vitro Bioaccessibility Data

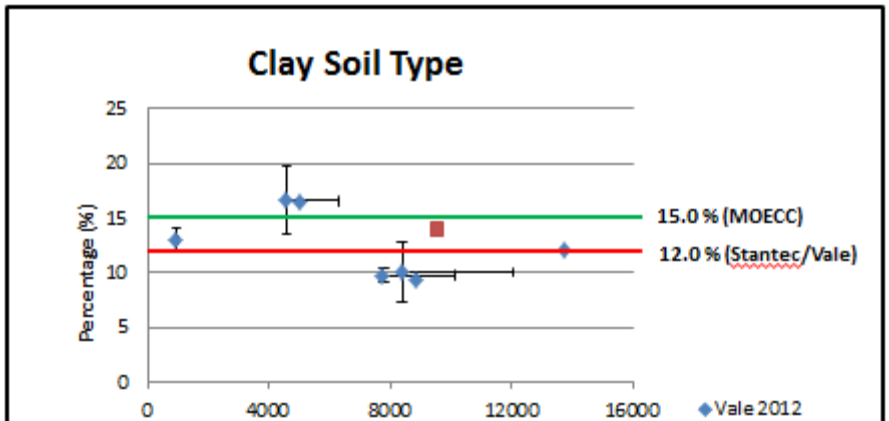
As with the fill soil type, many of the clay soil samples were taken from the same sampling location suggesting a greater number of soil locations than actually tested and raising concerns with treating the bioaccessibility estimates from the same location as independent discrete samples. As a consequence, the clay bioaccessibility data were re-analyzed by MOECC by sample location (MOECC Figure C2). It should also be noted that the amount of bioaccessibility information for the clay soils is vastly improved over previous versions of the CBRA. Instead of only one soil location, information is now available for 8 locations.

Vale Response: Vale recognizes that these samples were from a small number of test pits. The samples were archived and had been characterized in the CBRA and were available to conduct a bioavailability study.

Clay Soil Type: Re-analysis of the ROB

Contrary to the results for the fill soil, there does not appear to be a relationship between Ni bioaccessibility and soil Ni concentrations. However, as with the fill soil, MOECC believes that a reasonable conservative estimate is to use the 95% UCLM. Using all of the bioaccessibility data (including the data from Vale 2012) results in a 95% UCLM of 15% for clay soils (see MOECC Figure C2 and Table C3 below). Note: this recommended bioaccessibility estimate captures the range of bioaccessibility for clay soils with Ni concentrations <8,000 mg/kg (which range from 10 to 17%).

MOECC Figure C2



MOECC Table C3: The following data was used to determine the clay soil type bioaccessibility:

		CBRA Report (2014)		Re-analysis(MOECC)		
In-vitro Experiment	**Sample Location**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**	
Vale (2012)	TP3	8912	9.4	8912	9.4	
Vale (2012)	TP5	9527	10.2	7775 ± 2344	9.8 ± 1.0	
Vale (2012)	TP5	8686	10.1			
Vale (2012)	TP5	5112	9.1			
Vale (2012)	TP6	13798	12	13798	12.0	
Vale (2012)	TP-J2	5816	14.5	4579 ± 1749	16.7 ± 3.0	
Vale (2012)	TP-J2	3342	18.8			
Vale (2012)	TPK2-1	968	12.2	939 ± 40	13.0 ± 1.0	
Vale (2012)	TPK2-1	911	13.8			
Vale (2012)	TP206	12495	7.9	8399 ± 3631	10.1 ± 2.8	
Vale (2012)	TP206	5572	9.1			
Vale (2012)	TP206	7131	13.2			
Vale (2012)	Hruska	5019	16.4	5019	16.4	
JWL (2002)	G3A	9580	14	9580	14.0	
			12		12.7	**Average (Mean)**
					15.0	**95th UCLM**
					16.7	**95th ile**

Summary Point Estimate of Bioaccessibility for Clay Soil Type

For the HHRA, the 95th UCLM of the Fill soil type data at 15.0% bioaccessibility is supported as a CTE estimate. For the sensitivity analysis, the 95th percentile at 16.7 % bioaccessibility is supported as a RME estimate.

Vale Response: Comment received.

Organic Soil Type: Inappropriate Analysis of in-vitro Bioaccessibility Data

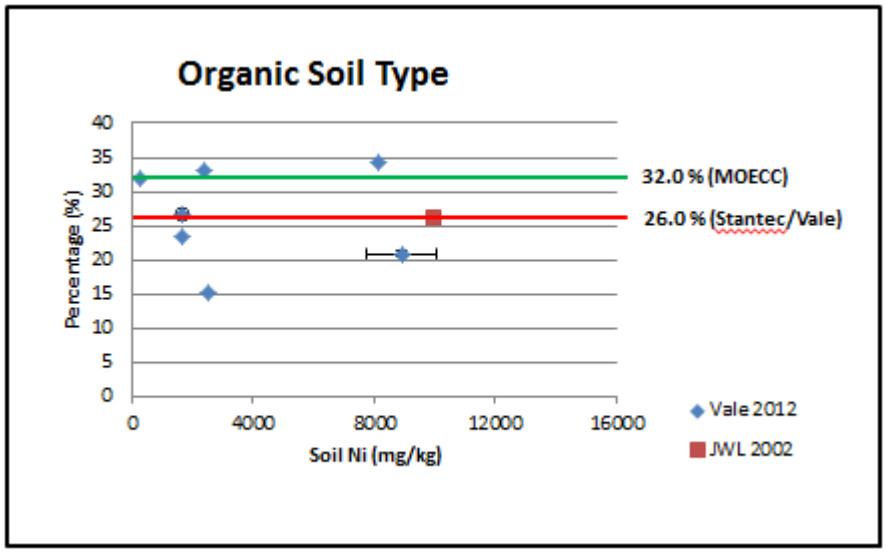
As with the fill soil type, many of the organic soil samples were taken from the same sampling location suggesting a greater number of soil locations than actually tested and raising concerns with treating the bioaccessibility estimates from the same location as independent discrete samples. As a consequence the organic bioaccessibility data were re-analyzed by MOECC by sample location (MOECC Figure C3). It should also be noted that the amount of bioaccessibility information for the organic soils is vastly improved over previous versions of this report. Instead of only one soil location,

information is now available for 8 locations.

Organic Soil Type: Re-analysis of the ROB

As observed for the clay soil, there does not appear to be a relationship between Ni bioaccessibility and soil Ni concentrations. However, as with the fill soil, MOECC believes that a reasonable conservative estimate is to use the 95% UCLM. Using all of the bioaccessibility data (including the data from Vale 2012) results in a 95% UCLM of 32% for organic soils (see MOECC Figure C3 and MOECC Table C4 below). Note: this recommended bioaccessibility estimate captures the range of bioaccessibility for organic soils with Ni concentrations <8,000 mg/kg (which range from 15 to 35%).

MOECC Figure C3



MOECC Table C4: The following data was used to determine the organic soil type bioaccessibility:

		CBRA Report (2014)		Re-analysis(MOECC)	
In-vitro Experiment	**Sample Location**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**	**[soil]Ni mg/kg**	**Bioaccessibility (%)**
Vale (2012)	Groetlarr	9754	20.6	8921 ± 1177	21 ± 0.5
Vale (2012)	Groetlaar	8089	21.3		
Vale (2012)	SS20 Low Organic	239	32.0	239	32.0
Vale (2012)	SS27 Med Organic	1640	23.5	1640	23.5
Vale (2012)	SS25 V.High Organic	8125	34.4	8125	34.4
Vale (2012)	Ni 1000c	2547	15.3	2547	15.3
Vale (2012)	TP-R4	2369	33.1	2369	33.1
Vale (2012)	TP-S	1980	26.0	1668 ± 210	26.7 ± 0.9
Vale (2012)	TP-S	1527	27.0		
Vale (2012)	TP-S	1590	27.8		
Vale (2012)	TP-S in Qe	1574	25.9		
JWL (2002)	G1A	9980	26.0	9980	26

	26		26.5	**Average (Mean)**
			32.0	**95th UCLM**
			34.4	**95th ile**

Summary Point Estimate of Bioaccessibility for Organic Soil Type

For the HHRA, the 95th UCLM of the Fill soil type data at 32.0% bioaccessibility is supported as a CTE estimate. For the sensitivity analysis, the 95th percentile at 34.4% bioaccessibility is supported as a RME estimate.

Vale Response: Comment received. Vale understands that the organic muck soils have higher bioavailability than clay or fill. A potential mechanism responsible for this has been proposed in Dutton et al. (2020).

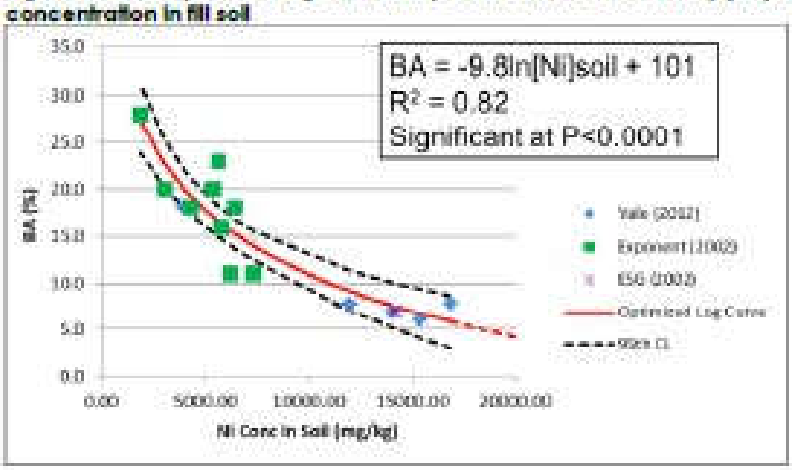
3. ***Other factors that combined reduce the overall confidence in the proposed bioavailability and bioaccessibility estimates.***

The ministry has low confidence in the revised CBRA report for the changes made to determine the Relative Oral Bioavailability based on Bioavailability and Bioaccessibility estimates for the following reasons:

- Only summary information is provided for both the bioavailability and bioaccessibility estimates in the revised CBRA; this includes new information (Vale 2012) presented for the first time to the MOECC. For example, the updated CBRA report does not provide any information on study design, lab reports (SOPs, QA/QC procedures) and methods of analysis.
- There are still inconsistencies in the reporting of sample information. For example, the sample locations as reported in Tables (e.g. Tables 3E-1 and 3E-2) is sometimes different than those indicated in Figures (e.g. map Figures 3E-3 and 3E-3).
- Figure 3E-4 line (including r^2) could not be reproduced by the ministry based on the information provided in Tables 3E-2 and 3E-3 (Figure 3E-4 provided below followed by the ministry's re- analysis in MOECC Table 5C).

Screen Grab: Figure 3E-4: Optimized log relationship between bioaccessibility (BA) of nickel and the concentration in fill soil (Updated Report 2014)

Figure 3E-4: Optimized log relationship between bioaccessibility (BA) of nickel and the concentration in fill soil



MOECC Table 5C: Ministry Re-analysis of fill soil bioaccessibility

	Log	R^2	
Fill Bioaccessibility with MOE (Exponent, 2002)	BA = -9.8 In {Ni} soil + 101	0.82	Reported
	BA = -9.98 In {Ni} soil + 101.9	0.717	Re-calculated
	BA = 32.99 - 0.003796 x [Ni] soil + 1.336E-7 x ([Ni] soil)^2	0.756	Re-calculated

Note: Even though the reported relationship in the CBRA report could not be reproduced; the potential change does not result in a significant difference in the bioaccessibility estimates, but a lower confidence in the equation (R^2). The Line of Best Fit statistics have not been used to determine the quadratic line, but it appears to have a better fit to the data.

Estimated Bioaccessibility (%) using the recalculated new line (Ln)

	Bioaccessibility (%)	
[soil]Ni mg/kg	**Measured**	**Calculated**
7310	11	12.4
1840	28	26.5
5370	20	16.4
6410	18	14.1
5620	23	15.9
5730	16	15.6
6200	11	14.6
5290	20	16.6
3040	20	22.7
4270	18	19.2
13848	6.7	6.0
17420	7.7	7.3
8680	7.8	10.1
8489	5.8	10.4
3265	17	22.0
11600	6.9	6.9

Discussion

Several meetings were held between Vale and the MOECC on Ni speciation work to investigate if distance from the refinery (i.e., the source) was related to Ni solubility (i.e., bioaccessibility) due in part to a decrease in particle size with distance (since smaller particles travels farther in air) and Ni speciation of these particles. In other words, the closer a soil is to the facility, the more likely it is to have larger particles associated with lower soluble Ni metal. Thus, the highest concentrations of soil Ni close to the facility may not be as bioaccessible as lower soil Ni concentrations farther from the facility. Based on the analysis conducted with this data, it appears to be the case for Fill soil where Ni bioaccessibility in soils with Ni greater than 8,000 mg/kg is much lower (about 7%) than Ni bioaccessibility estimates for soils with Ni less than 8,000 mg/kg (range from 10 to 28%). While this would be expected to hold true for all three soil types, the analysis was not able to support this for the clay or organic soils.

Vale Response: Comment received.

Summary Estimate of Bioaccessibility data for Fill Soil:

The ministry's re-analysis supports the Fill soil equation of BA = 32.99 - 0.0003796 x [Ni]soil + 1.336E-7 x $([Ni]soil)^2$, based on individual samples; not considering sample location. While the upper confidence limits for this relationship could be used to develop a site-specific bioaccessibility estimate for any given soil Ni concentration, the Ministry recommends that the 95th UCLM of 22% be used instead (as discussed previously). A comparison of the bioaccessibility estimates from the updated CBRA report and the ministry's re-analysis is provided below (MOECC Table C6).

MOECC Table C6: Overall ROB Recommendations and Comparison Chart:

Soil Type		Bioaccessibility/ROB		
		CBRA Report (2014)	Re-analysis (MOECC)	Estimate
Fill	HHRA	5.8 %	21.0 %	CTE
		= -9.8 In {Ni} soil + 101	BA = 32.99 - 0.0003796 x [Ni]soil + 1.336E-7 x $([Ni]soil)^2$	CTE
	Sensitivity	8.7 %	28.0 %	RME
Clay	HHRA	9.4 %	15.0 %	CTE
	Sensitivity	12 %	16.7 %	RME
Organic	HHRA	22 %	32.0 %	CTE
	Sensitivity	26 %	34.4 %	RME

References:

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SLI 2000b. Springborn Laboratory Inc.An Oral (Gavage) Two-Generation Reproduction Toxicity Study in Sprague- Dawley Rats with Nickel Sulfate Hexahydrate. Final Report. Springborn Laboratory, Inc. Study No. 3472.4. Submitted to: NiPERA, Inc., Durham, North Carolina, USA.

Appendix D: Outdoor Soil to Indoor Dust Ratio in Port Colborne

Overall Conclusions on the outdoor soil to indoor dust ratio:

Based on a limited number of samples, the ratio between Ni in indoor dust and Ni in soil was estimated in this CBRA to be 0.2 (i.e., dust contains 20% of the total Ni that is found in soil from the Port Colborne community). This ratio was used in the CBRA to estimate the Ni concentration of indoor dust from measured Ni concentrations in soil as part of developing the RBSC. The ministry has concerns with this ratio primarily because the dataset is too small to develop a robust estimate and also because the ratio of Ni in indoor dust to Ni in soil is often much higher than 0.2 below a soil Ni concentration of 2,000 mg/kg.

The ministry agrees that given the uncertainty associated with the limited data available, a ratio of 0.2 could be considered an acceptable qualitative value for characterizing soil with Ni concentrations greater than 2,000 mg/kg. However we do not support using this ratio for soils with Ni concentrations less than 2,000 mg/kg. Instead, MOECC calculated a ratio of Ni in indoor dust to Ni in outdoor soil of 0.56 for Ni concentrations < 2,000 mg/kg using a modified dataset of the CBRA's dust and soil data.

MOECC notes that while the ratio of 0.2 may be acceptable at the RBSC proposed in the CBRA (e.g., 48,000 mg/kg for the Rodney Street community), it is inappropriate to use for developing a RBSC at soil Ni concentrations less than 2,000 mg/kg. Quantitatively, the use of this ratio is limited for the following reasons: (1) it was based on a limited number of paired samples with high Ni soil concentrations (n=6); (2) approximately 65% of the data has a ratio greater than 0.2); and (3) it does not account for the variability across the distribution of the data.

For Ni concentrations less than 2,000 mg/kg, the ratio of 0.56 determined by the MOECC lies between the generic default values of 0.39 used in the Rodney Street Risk Assessment Report (MOE, 2002) and a ratio of 0.7 used in the US EPA's Integrated Exposure and Uptake Biokinetic (IEUBK) model for lead exposure to children (US EPA, 2002). MOECC is aware that even higher indoor dust to outdoor soil ratios in residential areas has been reported in the literature. However, these higher estimates are derived at relatively low soil Ni concentrations (as compared to the large range of elevated Ni soil concentrations observed in Port Colborne soil) and are often influenced by indoor sources of Ni that are independent of the outdoor soil.

The ratio used for Ni in indoor dust to outdoor soil is also much lower than that observed for the other compounds of concern in this CBRA. For example, the concentration of arsenic in dust is 5 times the levels in soil. Similarly, copper dust concentrations are 2 times and cobalt dust concentrations are equal to the outdoor soil concentrations. These higher ratios for the other COCs are likely due to the fact that the soil concentrations are not as elevated (when compared to Ni) than background levels and do not reflect the wide range of soil concentrations as observed with Ni. MOECC is also aware that a higher residential ratio of Ni in indoor dust of 4.3 times the outdoor soil concentration was determined as part of the Sudbury Soils Study from a much larger dataset (n = 88; SARA, 2005). However, this higher ratio for Sudbury (which ranged from 1.5 to 32 times the outdoor soil) than observed for Port Colborne would be expected as the Sudbury data had lower Ni soil concentrations (from 22 to 3,390 mg/kg; mean = 480 mg/kg), and there continues to be an active sources of Ni from aerial emissions in Sudbury. Overall, despite the limited paired samples from the Port Colborne dataset (n=15 from zones 1 and 2), a site-specific ratio calculated from the limited available data is preferred than using a literature default value.

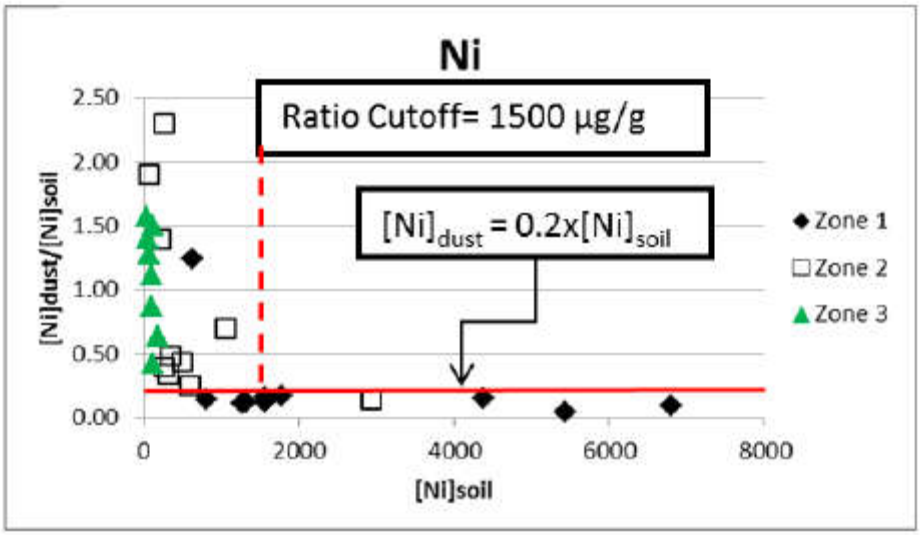
In summary, the basis of a ratio of 0.2 proposed by Stantec is limited and at best can be used to predict Ni in dust for soil Ni concentrations greater than 2,000 mg/kg. MOECC supports the use of a Ni in indoor dust to Ni in outdoor soil ratio of 0.56 when soil Ni concentrations are less than 2000 mg/kg.

Vale Response: Vale accepts the Ministry's analysis, given the limited data available.

Limitations in Data and Analysis

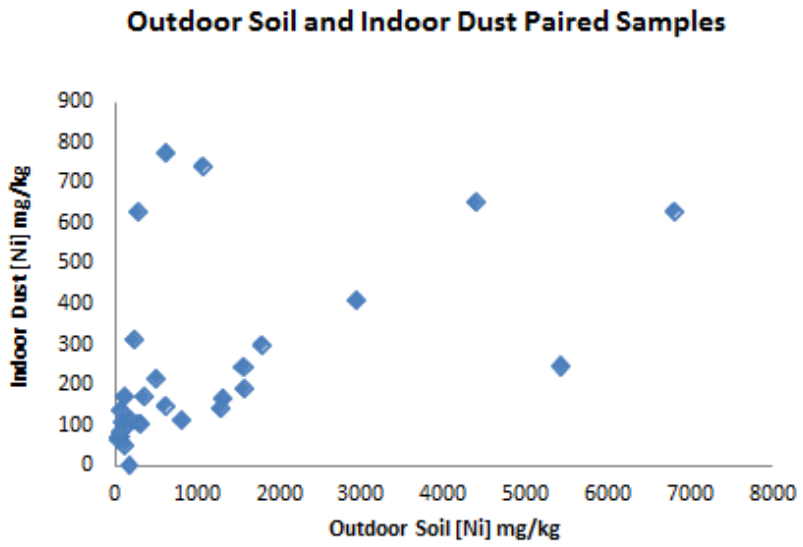
In MOECC Figure D1 (Concentration Ratio Plots for COCs - Nickel), the ratio of 0.2 proposed by Stantec is represented by a red line. As noted in the CBRA report, based on a "visual inspection" of these 28 co-localized soil and indoor dust samples, Stantec identified a Ni concentration of 1,500 mg/kg as a inflection point or as a "ratio cut-off" and selected a ratio of 0.2 that appears to reflect an upper estimate of the 6 datapoints above this concentration.

MOECC Figure D1 (Figure 3B.1; Screen Grab Stantec 2014, Appendix 3B pp 1.12)



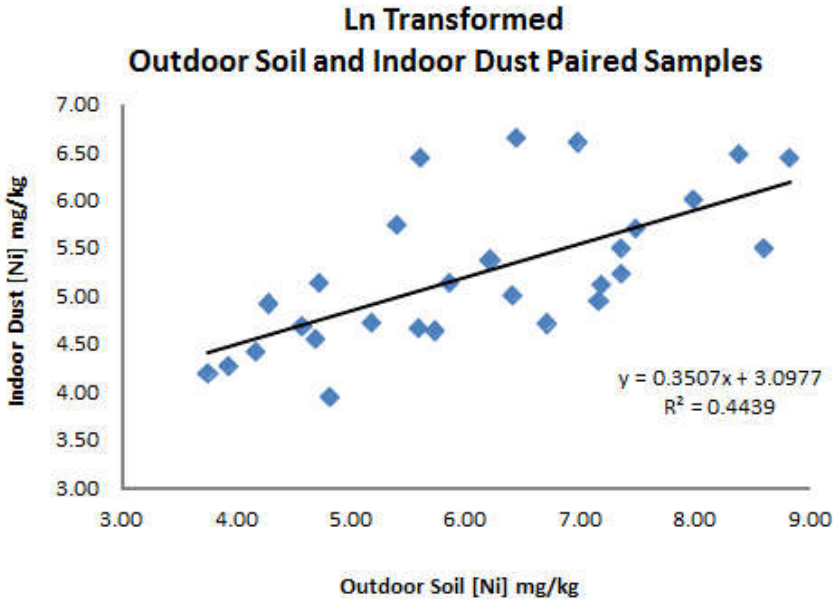
However, most of the data is for soil Ni concentrations below 1,500 mg/kg (n=21 of 28 samples). The large variability of the Ni in indoor dust to Ni in outdoor soil ratio in these samples is also clearly evident at Ni concentrations < 1,500 mg/kg ranging from 0.1 to 2.3. The limited number of samples at the higher soil Ni concentrations (n = 6 for Ni > 1,500 mg/kg; n = 4 for Ni > 2,000 mg/kg) is insufficient to properly characterize the variability and uncertainty inherent in this ratio and severely limits meaningful statistical interpretation of this data at these Ni concentrations. An indication of this variability can be seen when the actual dust and soil data is plotted (MOECC Figure D2).

MOECC Figure D2



While a weak linear relationship can be determined ($r^2 = 44$) when comparing the natural log of Ni in indoor dust to the natural log of Ni in outdoor soil (MOECC Figure D3), this plot clearly illustrates the high variability in this relationship.

MOECC Figure D3



Ni Concentration at Inflection Point or "Ratio Cut Off"

In the CBRA update report, Stantec states that the ratio of 0.2 is "conservative for predicting the concentrations in dust when the concentrations in soil exceed the ratio cut-off in each CR plot. Ratio cut-offs were established by determining the soil concentration where the data clearly

departs from the horizontal relationship." However, since this ratio cut-off was based on visual observation and not on statistical analysis, the ratio of 0.2 and the "ratio cut-off" of 1,500 mg/kg can't be supported quantitatively. However, qualitatively, MOECC recognizes that:

- At low Ni outdoor soil concentrations, other indoor sources of Ni can contribute to the observed higher ratios of Ni in indoor dust to Ni in outdoor soil concentrations and likely contribute to the higher variability of the data, and
- At higher Ni outdoor soil concentrations, indoor sources of Ni are less influential

Based on this qualitative assessment, it is reasonable to expect that a decrease in Ni concentrations in dust to soil ratios would be expected as soil Ni concentrations increases over the observed range of soil Ni concentrations. However, it is not clear where the cut-off should be that distinguishes between high and low soil Ni concentrations. Based on the limited data, it appears that 1,500 mg/kg may be too low as out of the 6 datapoints between 1,000 and 2,000 mg/kg, one value greatly exceeds this ratios (i.e., sample #205: soil = 1,064 mg/kg, ratio = 0.7). As a result, MOECC believe that the ratio cut-off point should be 2,000 mg/kg instead of 1,500 mg/kg. Despite the limited number of paired samples, the ratio of 0.2 is greater than the maximum calculated ratio of 0.16 observed in this dataset. Therefore, MOECC recommends using the ratio of 0.2 only if soil Ni concentrations exceed 2,000 mg/kg.

Vale Response: Vale accepts the Ministry's analysis, given the limited data available.

Re-analysis of the Paired Outdoor Soil to Indoor Dust Ratio

In order to address concentrations below 2,000 mg/kg, the paired dust and soil data was re-analyzed (raw data provided in MOECC Table D1). Only soil data from Zone 1 and 2 with soil Ni concentrations greater than 200 mg/kg but less than 2,000 mg/kg were used in this re-analysis to minimize the likelihood of other indoor sources of Ni influencing the results and to focus on the concentration range of interest. The modified dataset had a smaller number of paired samples (n=15) with soil Ni concentrations ranging from 222 to 1,783 mg/kg. The overall average soil and dust Ni concentration was calculated to be 835 and 291 mg/kg respectively.

Based on this re-analysis, the average (arithmetic mean) of 0.56 is recommended by MOECC for use in the calculation of the RBSC when soil Ni concentrations are less than 2,000 mg/kg. Although a higher dust to soil ratio is expected for homes with soil Ni concentrations below 200 mg/kg (as high as 2.3), the overall contribution of Ni in dust to overall Ni exposure at this soil Ni concentration is relatively minor.

Overall, MOECC recognizes that there is uncertainty with this estimate and that further paired sampling would be required to better characterize the relationship between Ni concentrations in indoor dust and outdoor soils.

MOECC Table D1 - Data used to determine the outdoor soil to indoor dust ratio. Data was extracted From Table 3B.2: Concentration of paired samples of outdoor soil and indoor dust (vacuum samples of soft surface only) from Port Colborne homes.

	CBRA Report (2014)			**Re-analysis (MOECC)**		
Sample ID	Soil [Ni] (mg/kg)	Dust[Ni] (mg/kg)	Soil [Ni] / Dust [Ni]	Soil [Ni] (mg/kg)	Dust[Ni] (mg/kg)	Soil [Ni] / Dust [Ni]
101	1319	167	0.13	1319	167	0.13

103	6800	629	0.09				
104	5428	247	0.05				
106	1560	245	0.16	1560	245	0.16	
107	625	775	1.24	625	775	1.24	
108	1278	141	0.11	1278	141	0.11	
109	1783	300	0.17	1783	300	0.17	
110	814	112	0.14	814	112	0.14	
112	4384	652	0.15				
113	1563	189	0.12	1563	189	0.12	
201	496	217	0.44	496	217	0.44	
202	2935	409	0.14				
203	603.5	150	0.25	603.5	150	0.25	
204	351	170	0.48	351	170	0.48	
205	1063.5	743	0.7	1063.5	743	0.7	
206	72.25	138	1.91				
207	272	628	2.31	272	628	2.31	
208	222.75	312	1.4	222.75	312	1.4	
209	268.25	106	0.4	268.25	106	0.4	
210	310	104	0.34	310	104	0.34	
301	96.5	108	1.12				
302	177.75	113	0.64				
304	109	95	0.87				
305	123.5	52	0.42				
306	172	N/A	N/A				
307	42.5	67	1.58				
308	51	72	1.41				
309	113	170	1.5				
310	64.75	83	1.28				
				835	291	**0.56**	**Average**

Vale Response: Vale accepts the Ministry's analysis, given the limited data available.

Appendix E: Soil Ingestion Rate Exposure Assumption

Overall Conclusions on Soil Ingestion Rate:

The ministry has considered the alternative incidental soil ingestion rate (SIR) of 110 mg/day for the toddler receptor and find that it is reasonable for use in the CBRA. However, this represents a Central Tendency Exposure (CTE) estimate in the calculation of exposure from the soil and dust pathways. The ministry also considers the SIR of 200 mg/day to be valid for use in the CBRA as a Reasonable Maximum Exposure (RME) estimate. The SIR of 200 mg/day has been identified as conservative assumption (MOE, 2011) and MOECC maintains its use in the development of

Brownfields (O. Reg. 153/04) soil standard setting. The incidental SIR is the key exposure assumption used in the CBRA in estimating exposure from the combined soil and dust pathways. As the SIR does not distinguish between soil and dust it may be assumed for both the soil and dust exposure pathways using the 45:55 ratio as assumed in the US EPA's Integrated Exposure and Uptake Biokinetic (IEUBK) model for lead in children (US EPA, 2002). In addition, as done in the CBRA, the soil pathway may also be pro-rated for winter snow cover, where exposure to soil outdoors is considered negligible or zero.

It is recognised that the SIR inherently has limitations in estimating the amount of soil and dust ingested. In fact, the US EPA (2011) noted that the SIR has an overall "low" confidence rating. Given these limitations and based on the rationale provided by Stantec in the CBRA, the ministry can support using a SIR of 110 mg/day as a CTE in the CBRA. However, the ministry does not agree with the statement that "A soil/dust ingestion rate of 200 mg/day (MOE, 2011) for a toddler is not supported by current literature or recommendations by the US EPA (1997, 2011) and Health Canada (2009, 2012) for application as a chronic intake." It should be noted that the children's SIR in the US EPA's 2011 Exposure Factor Handbook recommends 100 mg/day (rounded from 110 mg/day) for ages 1 to <6 years as a population central tendency estimate. The upper percentile recommendation for soil and dust ingestion of 200 mg/day for 3 to < 6 years old is based on the 95th percentile value obtained from modelling (Ozkaynak et al., 2011) and from the 95th percentile value obtained from tracer studies (Stanek and Calabrese, 1995). In addition, the Ozkaynak et al., (2011) modelling (probablistic human-activity-based-physical model) was limited to the 3 to < 6 years old child; a younger age category would have been preferred, to cover the age around the 2 year old toddler when hand-to-mouth activity is assumed to be higher.

In consideration of the US EPA 2011 Exposure Factor Handbook, the OSWER Directive 9200.1-120 (2014) (which applies to Superfund sites) considers 200 mg/day as an upper bound estimate for residential child soil ingestion rate as their standard default exposure factor. This recommendation supersedes the Risk Assessment Guidance for Superfund: Human Health Evaluation Manual (RAGS), Parts A through E.

In summary, the MOECC supports the use of SIRs of 110 and 200 mg/day within the CBRA as CTE and RME estimates respectively. Furthermore, it is recommended that in calculating the RBSCs that the CTE and RME estimates are used to bracket risk management considerations.

Vale Response: Vale accepts the Ministry's analysis.

References:

MOE (Ministry of the Environment), 2011. Rationale for the Development of Soil and Groundwater Standards for Use at Contaminated Sites in Ontario, April 15, 2011. Standards \Development Branch. PIBS 7887e01.

Ozkaynak, H. 2011. "Modeled Estimates of Soil and Dust Ingestion Rates". Risk Analysis, 31 (4), 2011. 592-608

Stanek, EJ; Calabrese, EJ., 1995. "Daily estimates of soil ingestion in children". Environ Health Perspect 103(3):276−285.

US EPA (United States Environmental Protection Agency), 2002. User's Guide for the Integrated Exposure and Uptake Biokinetic (IEUBK) Windows Version -32 Bit Version, Environmental Protection Agency. EPA 540-K-01-005.

US EPA, 2011. Exposure Factors Handbook, Office of Research and Development, National

Center for Environmental Assessment. U.S. Environmental Protection Agency, Washington, D.C., EPA/600/R-06/052F.

US EPA, 2014. OSWER Directive 9200.1-120 Human Health Evaluation Manual, Supplemental Guidance: Update of Standard Default Exposure Factors, Office of Soil Waste and Emergency Response. U.S. Environmental Protection Agency, Washington, D.C .

Annex 1. Natural Environment ERA Additional Details

As the Ministry has pointed out in comments, the original CBRA Natural Environment Risk Assessment did not evaluate a worst-case scenario for terrestrial ecological risk. Rather, more of a central tendency estimate of exposure across the entire area of deposition was assessed, so risks associated with exposures in the areas of highest contamination, such as woodlot #17 (the "Reuter Road" woodlot) were not calculated, and the risk estimates were underestimated for such sites. The Update Report proceeded to estimate risk for the areas of highest contamination, but the use of the MEP approach did not characterize the worst-case risk. In this annex, the tables below provide an assessment of the worst-case risk expected in the terrestrial natural environment of the Port Colborne area. Several other ancillary issues are also discussed in this annex, in reference to Ministry comments in the main body of the comment-response dialogue above.

In relation to comment #18 above, Table A1-1 provides the 95% UCLM (calculated in Excel), which becomes 2,943 mg Ni/kg soil with these two data points (I-H-2 and I-H-4) included and with three samples (CS-H-7, CS-H-8, and CS-H-9) removed, as their Ni concentrations (364, 410, and 355 mg/kg, respectively) were clearly not from the same population of contamination as the other soil samples in the data set. In addition, an organic soil (denoted as "earthworm soil" and containing 2,971 mg Ni/kg) that was orally dosed to rats by gavage in a bioavailability study conducted by Vale has also been included in Table A1-1 (Dutton et al., 2019). Risk estimates in this response to comments consider this new value (2,943 mg/kg rather than the 2,404 mg/kg value used in the Update Report). In addition, earthworms were collected from the same location from which the organic soil was collected and their guts were allowed to clear so that no soil was present. These worms were pooled and homogenized and orally dosed to rats by gavage. The Ni content of these gut-cleared worms was 6.9 ± 1.0 mg/kg (wet weight) and, coincidentally, the bioavailability was 6.9% (95% CI [2.27, 11.48]) (Dutton et al., 2019).

Table A1-1. Soil [Ni] (mg/kg) revised fromTable B-2 of Stantec 2014 CBRA Update Report	
Sample	Nickel
CS-H-4	2460
CS-H-5	2000
I-H-3	1860
I-H-5	4310
OS-H-1	1350
OS-H-2	1550
OS-H-26	1770
OS-H-27	935
OS-H-28	2000
OS-H-29	2000
OS-H-3	2900
I-H-2	3790
I-H-4	2600
Earthworm Soil	2971
OS-H-6	3820
Average	2421
S.D.	943
n	15
95% C.I.	522
Upper 95% UCLM	**2943**

The Ni TRVs commonly used for ecological receptors are quite outdated by now. The NOAEL- and LOAEL-derived TRVs from Sample et al. 1996 (Toxicological Benchmarks for Wildlife: 1996 Edition) are based on the Ambrose et al. (1976) study, and the "O'Dell" TRV used by CCME and promoted by the Ministry in its comments are no longer relevant. Ecological risks due to Ni should be assessed using a TRV derived from the Springborn reproductive studies, just as human health risks are. Jacques Whitford initially attempted to use a TRV derived in such a way in the original Port Colborne Ni ERA, but derived it on a nickel sulphate hexahydrate basis, not on a Ni basis, the latter being the appropriate approach, given that we are interested in Ni, not NSHH.

In Table A1-2, the post-implantation and perinatal loss (PPL) data in their totality for the three components of the overall Springborn 2-generation reproductive toxicity studies are provided. The pooled control data (second last row of Table A1-2) are the most appropriate for identifying the NOAEL and LOAEL doses to use for ecological risk assessment.

Table A1-2. Post-implantation and perinatal loss data from the Springborn Ni reproductive toxicity studies used to derive mammalian TRVs for the ecological setting.

Study	Dose (mg Ni/kg/d) (in addition to baseline dietary exposure)	Post-implanation and perinatal loss (PPL) (%)	95% Confidence Interval	Lower 95% confidence limit	Upper 95% confidence limit
F0 Generation (dose range-finding study)	0 (controls)	2.1	3.1	-1.0	5.2
F0 Generation (dose range-finding study)[1]	2.2	4.3	3.8	0.5	8.14
F0 Generation (dose range-finding study)	4.4	10.4	8.2	2.2	18.6
F0 Generation (dose range-finding study)	6.6	14.4	10.6	3.8	25
F0 Generation (dose range-finding study)	11	17.5	11	6.5	28.5
F0 Generation (dose range-finding study)	16.5	36	22.1	13.9	58.1
F1 generation	0 (controls)	6.6	3.1	3.5	9.7
F1 generation	0.22	10.9	7.7	3.2	18.6
F1 generation	0.55	8.1	4	4.1	12.1
F1 generation	1.1	10.2	4.5	5.7	14.7
F1 generation	2.2	14.6	5.7	8.9	20.3
F2 generation	0 (controls)	5.9	2.5	3.4	8.4
F2 generation	0.22	9.3	6.2	3.1	15.5
F2 generation	0.55	8.8	3.5	5.3	12.3
F2 generation	1.1	8.6	2.8	5.8	11.4
F2 generation	2.2	9.9	2.8	7.1	12.7
Pooled controls (F0, F1, and F2)	0 (controls)	5.7	1.7	4.0	7.4
From the Literature	Historical Controls[2]	8.13	8.13	8.02	8.24

1. One dam (#204) at this dosing level lost all pups on lactation day 0 and was excluded from analysis. Had that dam been included, the average and 95% C.I. would become 16.2 and 26.7, respectively (which also would have overlapped the control confidence limits - i.e. were not different from controls).

2.. The historical control data are from 3541 pregnant female rats from 209 studies, as compiled by Lang (1993).

The upper confidence limit for the pooled controls (7.4 %) does not overlap with the lower confidence limit for the 16.5 mg/kg/d dose level from the F0 generation (13.9%), making 16.5 mg/kg/d the LOAEL. The upper confidence limit for the pooled controls (7.4 %) does overlap with the lower confidence limit for the 11 mg/kg/d dose level from the F0 generation (6.5 %), making 11 mg/kg/d the NOAEL.

In Tables A1-3-A1-5, below, risk scenarios are presented for the woodlot, while in Tables A1-6-1-A8 contain calculations for the adjacent field conditions. Three receptors were selected for these comparisons: the meadow vole (Tables A1-3 and A1-6), the short-tailed shrew (Tables A1-4 and A1-7), and the red fox (Tables A1-5 and A1-8). In these tables, the columns are notated so that the reader might scrutinize the calculations for accuracy.

In each of these pairs of tables, six individual scenarios have been selected. The specific changes

to each scenario are provided immediately below.

Exposure Point Concentration (EPC): In column B of Tables A1-3-A1-5 (woodlot scenario), the exposure point concentration(EPC) was the maximum soil [Ni] of 33,000 mg/kg, which was also the maximum value measured in the CBRA. In column B of Tables A1-6-A1-8, for the field scenarios, the EPC was the maximum soil Ni concentration from Table A1-1 (4,310 mg Ni/kg soil).

TRV: For each of the three pairs of scenarios in each table, different TRVs were used (column M) to allow some discussion of the estimated risk from the different scenarios. Scenarios 1 and 2 used the "O'Dell" TRV employed by the CCME, as mentioned by the Ministry. This TRV is not a scientifically sound TRV, in Vale's opinion, but is provided for context. Scenarios 3 and 4 use the NOAEL-based TRV of 11 mg/kg/d, derived above. Typically, NOAEL-based TRVs are used to assess risk to endangered or otherwise sensitive species. In this case, the NOAEL-based TRV is already for a sensitive endpoint (reproduction) and the TRV is essentially identifying the maximum dose that could be applied to a receptor without causing a significant increase in reproductive impairment among the population of exposed receptors. Scenarios 5 and 6 use the LOAEL-based TRV derived above (16.5 mg/kg/d). In this case, the LOAEL-based TRV would indicate moderate reproductive impairment would be possible under the scenario.

Bioaccessibility/Bioavailability: In all six tables, for each pair of scenarios using the same TRV, the bioavailability assumptions used for soil and food are provided in Columns C and H. In each table, scenarios 1, 3, and 5 use the Ministry-recommended values of 0.22 for soil bioaccessibility and 1.0 for food bioaccessibility, with the bioaccessible values representing a conservative representation of bioavailability. In scenarios 2, 4, and 6, the upper 95th percentile value of the measured bioavailability of organic soils from Dutton et al. (2019) was used (0.0067 (0.67%))[7]. The bioavailability of Ni from food (default value of 1.0 recommended by the Ministry) is replaced in the second pair of each scenario by the value 0.1148, which is the UCLM of bioavailability of gut-cleared earthworms gavage dosed to rats in Dutton et al. (2019). The bioavailability adjustments are discussed in detail in Annex 3.

The TRVs have similar values, so the Hazard Quotients are quite similar, although the O'Dell TRV is not particularly sound and should not be used. For both the woodlot scenarios and the field scenarios, the Hazard Quotients for all three receptors are heavily influenced by the bioavailability assumptions. A detailed discussion of bioavailability assumptions is provided in Annex 3. When appropriate bioavailability adjustments are used, the risks are seen to be acceptable for all six scenarios. It initially may seem counter-intuitive that such a very large soil Ni concentration (33,000 mg/kg) would have such low predicted risk for the woodlot scenarios, but it is because of the chemical forms of the Ni in the soil, which are so poorly bioavailable that this is the case. Failing to account for this factor leads to risk overestimation. Vale has

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[7] *The oral bioavailability of Ni in organic soil was determined for seven soil samples from three sampling locations in Dutton et al. (2019). Eight animals were dosed with each soil. The highest upper 95% confidence limit value values from among these organic soils was extracted from Table 5 of Dutton et al. (2019)) 0.67 (%) (i.e., 0.0067).*

continued to conduct research to understand the risks associated with the metal contamination caused by its refinery emissions between 1918 and 1984. These new risk calculations reflect Vale's continued learnings.

Scenario #	Organism	Site	(**A**) Soil Ingestion Rate (kg/d)	(**B**) Soil [Ni] (mg/kg)	(**C**) Bioaccessible/ Bioavailable Fraction	(**D**) (**A*B**) Total Daily Ni Intake from Soil (mg)	(**E**) (**A*B*C**) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Meadow Vole	Woodlot	0.00037	33000	0.22	12.197	2.683
2	Meadow Vole	Woodlot	0.00037	33000	0.0067	12.197	0.082
3	Meadow Vole	Woodlot	0.00037	33000	0.22	12.197	2.683
4	Meadow Vole	Woodlot	0.00037	33000	0.0067	12.197	0.082
5	Meadow Vole	Woodlot	0.00037	33000	0.22	12.197	2.683
6	Meadow Vole	Woodlot	0.00037	33000	0.0067	12.197	0.082

Scenario #	Organism	Site	(**F**) Food Intake Rate (kg/d) (fw basis)	(**G**) Food [Ni] (mg/kg fw)	(**H**) Bioaccessible/ Bioavailable Fraction	(**I**) (**F*G**) Total Daily Ni Intake from Diet (mg)	(**J**) (**F*G*H**) Bioaccessible Daily Ni Intake from Diet (mg)
1	Meadow Vole	Woodlot	0.0154	37.0	1	0.571	0.571
2	Meadow Vole	Woodlot	0.0154	37.0	0.1148	0.571	0.065
3	Meadow Vole	Woodlot	0.0154	37.0	1	0.571	0.571
4	Meadow Vole	Woodlot	0.0154	37.0	0.1148	0.571	0.065
5	Meadow Vole	Woodlot	0.0154	37.0	1	0.571	0.571
6	Meadow Vole	Woodlot	0.0154	37.0	0.1148	0.571	0.065

Scenario #	Organism	Site	(**K**) Body Weight (kg)	(**L**) ((**E+J**)/**K**) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(**M**) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(**N**) (**L/M**) **Hazard Quotient**
1	Meadow Vole	Woodlot	0.044	74.0	14.5	**5.10**
2	Meadow Vole	Woodlot	0.044	3.3	14.5	**0.23**
3	Meadow Vole	Woodlot	0.044	74.0	11.0	**6.72**
4	Meadow Vole	Woodlot	0.044	3.3	11.0	**0.30**
5	Meadow Vole	Woodlot	0.044	74.0	16.5	**4.48**
6	Meadow Vole	Woodlot	0.044	3.3	16.5	**0.20**

Table A1-3. Ecological Risk Assessment Woodlot Risk Scenarios for the Meadow Vole.

Scenario #	Organism	Site	(A) Soil Ingestion Rate (kg/d)	(B) Soil [Ni] (mg/kg)	(C) Bioaccessible/ Bioavailable Fraction	(D) (A*B) Total Daily Ni Intake from Soil (mg)	(E) (A*B*C) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Short-tailed shrew	Woodlot	0.000191	33000	0.22	6.3	1.4
2	Short-tailed shrew	Woodlot	0.000191	33000	0.0067	6.3	0.0
3	Short-tailed shrew	Woodlot	0.000191	33000	0.22	6.3	1.4
4	Short-tailed shrew	Woodlot	0.000191	33000	0.0067	6.3	0.0
5	Short-tailed shrew	Woodlot	0.000191	33000	0.22	6.3	1.4
6	Short-tailed shrew	Woodlot	0.000191	33000	0.0067	6.3	0.0

Scenario #	Organism	Site	(F) Food Intake Rate (kg/d) (fw basis)	(G) Food [Ni] (mg/kg fw)	(H) Bioaccessible/ Bioavailable Fraction	(I) (F*G) Total Daily Ni Intake from Diet (mg)	(J) (F*G*H) Bioaccessible Daily Ni Intake from Diet (mg)
1	Short-tailed shrew	Woodlot	0.00795	35.3	1	0.281	0.3
2	Short-tailed shrew	Woodlot	0.00795	35.3	0.1148	0.281	0.0
3	Short-tailed shrew	Woodlot	0.00795	35.3	1	0.281	0.3
4	Short-tailed shrew	Woodlot	0.00795	35.3	0.1148	0.281	0.0
5	Short-tailed shrew	Woodlot	0.00795	35.3	1	0.281	0.3
6	Short-tailed shrew	Woodlot	0.00795	35.3	0.1148	0.281	0.0

Scenario #	Organism	Site	(K) Body Weight (kg)	(L) ((E+J)/K) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(M) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(N) (L/M) **Hazard Quotient**
1	Short-tailed shrew	Woodlot	0.015	111.1	14.6	**7.61**
2	Short-tailed shrew	Woodlot	0.015	5.0	14.6	**0.34**
3	Short-tailed shrew	Woodlot	0.015	111.1	11.0	**10.10**
4	Short-tailed shrew	Woodlot	0.015	5.0	11.0	**0.45**
5	Short-tailed shrew	Woodlot	0.015	111.1	16.5	**6.73**
6	Short-tailed shrew	Woodlot	0.015	5.0	16.5	**0.30**

Table A1-4. Ecological Risk Assessment Woodlot Risk Scenarios for the Shrew.

Scenario #	Organism	Site	(A) Soil Ingestion Rate (kg/d)	(B) Soil [Ni] (mg/kg)	(C) Bioaccessible/ Bioavailable Fraction	(D) (A*B) Total Daily Ni Intake from Soil (mg)	(E) (A*B*C) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Red Fox	Woodlot	0.010800	33000	0.22	356.400	78.408
2	Red Fox	Woodlot	0.010800	33000	0.0067	356.400	2.388
3	Red Fox	Woodlot	0.010800	33000	0.22	356.400	78.408
4	Red Fox	Woodlot	0.010800	33000	0.0067	356.400	2.388
5	Red Fox	Woodlot	0.010800	33000	0.22	356.400	78.408
6	Red Fox	Woodlot	0.010800	33000	0.0067	356.400	2.388

Scenario #	Organism	Site	(F) Food Intake Rate (kg/d) (fw basis)	(G) Food [Ni] (mg/kg fw)	(H) Bioaccessible/ Bioavailable Fraction	(I) (F*G) Total Daily Ni Intake from Diet (mg)	(J) (F*G*H) Bioaccessible Daily Ni Intake from Diet (mg)
1	Red Fox	Woodlot	0.45	37.0	1	16.672	16.672
2	Red Fox	Woodlot	0.45	37.0	0.1148	16.672	1.914
3	Red Fox	Woodlot	0.45	37.0	1	16.672	16.672
4	Red Fox	Woodlot	0.45	37.0	0.1148	16.672	1.914
5	Red Fox	Woodlot	0.45	37.0	1	16.672	16.672
6	Red Fox	Woodlot	0.45	37.0	0.1148	16.672	1.914

Scenario #	Organism	Site	(K) Body Weight (kg)	(L) ((E+J)/K) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(M) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(N) (L/M) **Hazard Quotient**
1	Red Fox	Woodlot	4.5	21.1	14.6	**1.45**
2	Red Fox	Woodlot	4.5	1.0	14.6	**0.07**
3	Red Fox	Woodlot	4.5	21.1	11.0	**1.92**
4	Red Fox	Woodlot	4.5	1.0	11.0	**0.09**
5	Red Fox	Woodlot	4.5	21.1	16.5	**1.28**
6	Red Fox	Woodlot	4.5	1.0	16.5	**0.06**

Table A1-5. Ecological Risk Assessment Woodlot Risk Scenarios for the Red Fox.

Scenario #	Organism	Site	(A) Soil Ingestion Rate (kg/d)	(B) Soil [Ni] (mg/kg)	(C) Bioaccessible/ Bioavailable Fraction	(D) (A*B) Total Daily Ni Intake from Soil (mg)	(E) (A*B*C) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Meadow Vole	Field	0.00037	4310	0.22	1.593	0.350
2	Meadow Vole	Field	0.00037	4310	0.0067	1.593	0.011
3	Meadow Vole	Field	0.00037	4310	0.22	1.593	0.350
4	Meadow Vole	Field	0.00037	4310	0.0067	1.593	0.011
5	Meadow Vole	Field	0.00037	4310	0.22	1.593	0.350
6	Meadow Vole	Field	0.00037	4310	0.0067	1.593	0.011

Scenario #	Organism	Site	(F) Food Intake Rate (kg/d) (fw basis)	(G) Food [Ni] (mg/kg fw)	(H) Bioaccessible/ Bioavailable Fraction	(I) (F*G) Total Daily Ni Intake from Diet (mg)	(J) (F*G*H) Bioaccessible Daily Ni Intake from Diet (mg)
1	Meadow Vole	Field	0.0154	6.9	1	0.106	0.106
2	Meadow Vole	Field	0.0154	6.9	0.1148	0.106	0.012
3	Meadow Vole	Field	0.0154	6.9	1	0.106	0.106
4	Meadow Vole	Field	0.0154	6.9	0.1148	0.106	0.012
5	Meadow Vole	Field	0.0154	6.9	1	0.106	0.106
6	Meadow Vole	Field	0.0154	6.9	0.1148	0.106	0.012

Scenario #	Organism	Site	(K) Body Weight (kg)	(L) ((E+J)/K) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(M) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(N) (L/M) **Hazard Quotient**
1	Meadow Vole	Field	0.044	10.4	14.5	**0.72**
2	Meadow Vole	Field	0.044	0.5	14.5	**0.04**
3	Meadow Vole	Field	0.044	10.4	11.0	**0.94**
4	Meadow Vole	Field	0.044	0.5	11.0	**0.05**
5	Meadow Vole	Field	0.044	10.4	16.5	**0.63**
6	Meadow Vole	Field	0.044	0.5	16.5	**0.03**

Table A1-6. Ecological Risk Assessment Field Risk Scenarios for the Meadow Vole.

Scenario #	Organism	Site	(A) Soil Ingestion Rate (kg/d)	(B) Soil [Ni] (mg/kg)	(C) Bioaccessible/ Bioavailable Fraction	(D) (A*B) Total Daily Ni Intake from Soil (mg)	(E) (A*B*C) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Short-tailed shrew	Field	0.000191	4310	0.22	0.8	0.2
2	Short-tailed shrew	Field	0.000191	4310	0.0067	0.8	0.0
3	Short-tailed shrew	Field	0.000191	4310	0.22	0.8	0.2
4	Short-tailed shrew	Field	0.000191	4310	0.0067	0.8	0.0
5	Short-tailed shrew	Field	0.000191	4310	0.22	0.8	0.2
6	Short-tailed shrew	Field	0.000191	4310	0.0067	0.8	0.0

Scenario #	Organism	Site	(F) Food Intake Rate (kg/d) (fw basis)	(G) Food [Ni] (mg/kg fw)	(H) Bioaccessible/ Bioavailable Fraction	(I) (F*G) Total Daily Ni Intake from Diet (mg)	(J) (F*G*H) Bioaccessible Daily Ni Intake from Diet (mg)
1	Short-tailed shrew	Field	0.00795	6.9	1	0.055	0.1
2	Short-tailed shrew	Field	0.00795	6.9	0.1148	0.055	0.0
3	Short-tailed shrew	Field	0.00795	6.9	1	0.055	0.1
4	Short-tailed shrew	Field	0.00795	6.9	0.1148	0.055	0.0
5	Short-tailed shrew	Field	0.00795	6.9	1	0.055	0.1
6	Short-tailed shrew	Field	0.00795	6.9	0.1148	0.055	0.0

Scenario #	Organism	Site	(K) Body Weight (kg)	(L) ((E+J)/K) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(M) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(N) (L/M) **Hazard Quotient**
1	Short-tailed shrew	Field	0.015	15.7	14.6	**1.08**
2	Short-tailed shrew	Field	0.015	0.8	14.6	**0.05**
3	Short-tailed shrew	Field	0.015	15.7	11.0	**1.43**
4	Short-tailed shrew	Field	0.015	0.8	11.0	**0.07**
5	Short-tailed shrew	Field	0.015	15.7	16.5	**0.95**
6	Short-tailed shrew	Field	0.015	0.8	16.5	**0.05**

Table A1-7. Ecological Risk Assessment Field Risk Scenarios for the Shrew.

Scenario #	Organism	Site	(A) Soil Ingestion Rate (kg/d)	(B) Soil [Ni] (mg/kg)	(C) Bioaccessible/ Bioavailable Fraction	(D) (A*B) Total Daily Ni Intake from Soil (mg)	(E) (A*B*C) Total Daily Actual (Bioaccessible) Ni Intake from Soil (mg)
1	Red Fox	Field	0.010800	4310	0.22	46.548	10.241
2	Red Fox	Field	0.010800	4310	0.0067	46.548	0.312
3	Red Fox	Field	0.010800	4310	0.22	46.548	10.241
4	Red Fox	Field	0.010800	4310	0.0067	46.548	0.312
5	Red Fox	Field	0.010800	4310	0.22	46.548	10.241
6	Red Fox	Field	0.010800	4310	0.0067	46.548	0.312

Scenario #	Organism	Site	(F) Food Intake Rate (kg/d) (fw basis)	(G) Food [Ni] (mg/kg fw)	(H) Bioaccessible/ Bioavailable Fraction	(I) (F*G) Total Daily Ni Intake from Diet (mg)	(J) (F*G*H) Bioaccessible Daily Ni Intake from Diet (mg)
1	Red Fox	Field	0.45	6.9	1	3.105	3.105
2	Red Fox	Field	0.45	6.9	0.1148	3.105	0.356
3	Red Fox	Field	0.45	6.9	1	3.105	3.105
4	Red Fox	Field	0.45	6.9	0.1148	3.105	0.356
5	Red Fox	Field	0.45	6.9	1	3.105	3.105
6	Red Fox	Field	0.45	6.9	0.1148	3.105	0.356

Scenario #	Organism	Site	(K) Body Weight (kg)	(L) ((E+J)/K) Sum of Daily Oral Bioaccessible/ Bioavailable Ni from Soil and Food (mg/kg/d)	(M) Daily Toxicity Reference Vale (TRV) (mg/kg/d)	(N) (L/M) Hazard Quotient
1	Red Fox	Field	4.5	3.0	14.6	**0.20**
2	Red Fox	Field	4.5	0.1	14.6	**0.01**
3	Red Fox	Field	4.5	3.0	11.0	**0.27**
4	Red Fox	Field	4.5	0.1	11.0	**0.01**
5	Red Fox	Field	4.5	3.0	16.5	**0.18**
6	Red Fox	Field	4.5	0.1	16.5	**0.01**

Table A1-8. Ecological Risk Assessment Field Risk Scenarios for the Red Fox.

References

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Annex 2. Vale's Interpretation of TRV 11.

Vale has previously responded, in detail, to the Ministry's recommended TRV of 11 µg/kg body weight/day. A slide deck from a presentation previously made to the Ministry explaining Vale's stance is appended to this annex for reference. In addition, the following commentary is provided to reflect the new information available in the literature as well as work completed by Vale since the Ministry's comments were provided to Vale in 2016.

In 2020, the Human Toxicology and Air Standards (HTAS) Section, Technical Assessment and Standards Development Branch (TASDB) of the Ministry released an 'approved' oral TRV for Ni of 11 µg/kg/d, as per the document entitled: 'Human Health Toxicity Reference Value (TRVs) Selected for Use at Contaminated Site in Ontario' (MECP, 2020). The Ministry's rationale for the selection of this TRV was summarized in an earlier document entitled 'Toxicity Reference Value (TRV) Selections for Nickel (Ni) CAS# various' (MECP,2019), dated August 2019.

The Ministry's approved non-cancer oral TRV for Ni (of 11 µg/kg/d) is not robust because it failed to evaluate the underlying scientific data and relies on the work published by other regulatory agencies. More specifically, the MECP (2019) document indicates that the Ministry has relied upon four other regulatory TRV derivations, the California Environmental Protection Agency's child-specific Reference Dose (chRD) development document from 2005 (OEHHA, 2005), Health Canada's Ni TRV from its 2010 document (HC, 2010), California EPA's 2012 document (OEHHA, 2012), and the European Food Safety Agency's 2015 derivation (Fig. A2-1).

TRV SELECTION SUMMARY
Oral Chronic Non-Cancer

Evaluation Results	Agency /Year / TRV (mg/kg/d)	Notes	
Selected	**1.1 x 10^{-2} mg/kg/d: Cal EPA chRD 2005, HC CSD 2010, & Cal EPA chREL 2012**	Basis for Selection of TRV	Cal EPA chRD (2005), HC CSD (2010), Cal EPA chREL (2012), & EFSA (2015) are supportable with no issues of concern. Though normally a POD derived through BMD modelling would be preferred, since EFSA used the lowest BMDL rather than that with the best statistical, this TRV was not preferred over the others.
	2.8 x 10^{-3} mg/kg/d: EFSA 2015	Special Considerations	None

Fig. A2-1. TRV selection summary from MECP (2019). This table is an extract from the "TRV Selection Summary" Table provided in MECP (2019), but only includes the "selected" evaluation results. The evaluation results that the Ministry has considered to have concerns or some concerns have been excluded here, since they were ruled-out by the Ministry. Source: MECP (2019).

The TRVs published by HC (2010), OEHHA (2012), and EFSA (2015) have been evaluated previously by Vale and were shown to have significant issues. This information was given to the Ministry in the form of a presentation provided to Dr. Jim Gilmore on November 28, 2016 (Vale, 2016)[8]. As previously illustrated in Vale (2016), three of the TRV derivations cited in Fig. A2-1 are seriously flawed and are seen to not withstand scientific scrutiny. It should also be noted that EFSA was required to re-evaluate its 2015 assessment of nickel by the European

[8] ***Presentation is appended to this Annex.***

Commission. EFSA's draft reassessment was released in June, 2020 (EFSA, 2020).

The revised EFSA (2020) TDI value (tolerable daily intake) has been revised upwards from 2.8 to 13 µg/kg/d; however, like EFA's previous 2015 derivation, the new analyses (presented by EFSA and used to develop their draft 2020 TDI) is not transparent nor does it currently provide sufficient detail to facilitate an independent analysis to determine if the EFSA results can be replicated. The 2020 EFSA analyses are less preferred (scientifically) than the benchmark dose (BMD) derivation of Haber et al. (2017), which is completely transparent and, unlike EFSA's analyses, can be replicated by others. Haber et al. (2017) provided the raw data used in their analysis and transparent documentation of the methods used, enabling others to duplicate Haber's findings as a means of scrutinizing and verifying the methods and results. The Ministry's own 2019 Ni TRV derivation as cited in MECP (2019) makes no mention of this latest work (Haber et al., 2017) nor does it present an independent evaluation of the actual toxicity data obtained from the original sourced materials. The rationale provided by the MECP (2019) appears to rely on the interpretation and judgement put forward by other jurisdictions published, in some instances, more than a decade ago.

The issues of concern that Vale has presented previously regarding the Health Canada (HC, 2010), California EPA (OEHHA, 2012), and the European Food Safety Agency (EFSA, 2015) non-cancer Ni TRV derivations did not include the California EPA's chRD development document (OEHHA, 2005). As such, Vale's review of this information source (OEHHA, 2005) is provided here to complete the discussion.

OEHHA (2005) in turn cited an earlier California EPA document – the PHG (Public Health Goal) for Ni in drinking water (OEHHA, 2001) as the source of a NOAEL value (of 1.1 mg Ni/kg body weight/day) that OEHHA (2005) subsequently used to support its chRD, and which the Ministry has accepted via serial citation. It is therefore necessary to evaluate the OEHHA (2001) PHG (primary health goal) derivation, as it represents the first identified regulatory use of the reproductive toxicity studies conducted by Springborn Labs on behalf of the Nickel Producers Environmental Research Association (NiPERA). A 1-generation dose range-finding (DRF) study of nickel sulphate hexahydrate (NSHH - $NiSO_4 \cdot 6H_2O$) was first conducted using a broad range of doses and moderate replication (SLI, 2000a). These results guided the selection of doses for the definitive 2-generation study, which had a smaller range of doses and much greater replication (SLI, 2000b).

The Springborn DRF study (SLI, 2000a) reported the occurrence of significant increases in the incidence of pup mortality on lactation day 0 at all treatment levels, except the 50 mg/kg/d treatment (p. 24 of SLI, 2000a). It is likely that this statistic was the source of the stated LOAEL reported by OEHHA (2001), as the raw mortality incidence in the lowest treatment level (10 mg/kg/day as $NiSO_4 \cdot 6H_2O$ or 2.2 mg/kg/day as Ni) was reported to be significantly different from control mortality in Table 17 of SLI (2000a). However, there are errors in Table 17 of the Springborn DFR study (SLI, 2000a) – the mortality numbers for most of the treatment levels were incorrectly reported in this table – this becomes evident when cross referencing the data presented in Table 17 with the raw data presented in Appendix U of SLI (2000a). Table A2-1 (below) provides pup mortality data on lactation day 0 as well a*s the associated average values*

and 95% confidence limits for the dose groups sourced from Appendix U of the Springborn DRF study (SLI, 2000a). These data (as presented in Table A2-1) allow the reader to calculate these values for themselves. It can be seen that for the 10, 20, and 30 mg/kg/d dose groups, the lower confidence limits overlap with the upper confidence limit for the controls, indicating that pup mortality among these NSHH-dosed rats was actually not different from that observed in the control animals not exposed to NSHH. As such, based on a review and analysis of the raw data (Table A2-1) extracted from the Springborn DRF study (SLI, 2000a), the NOAEL for perinatal mortality of NSHH appears to be <u>30 mg/kg/d NSHH</u>, as pup mortality rates in this group are no different from those observed in the control group as evident from the overlapping confidence intervals.

OEHHA (2001) incorrectly asserted that there was increased perinatal mortality at the 10 mg NSHH/kg/day group level, presumably as a result of erroneous data presented in Table 17 of the Springborn DFR study (SLI, 2000a) and, therefore, considered 10 mg NSHH/kg/day to be the LOAEL for perinatal mortality. This incorrect assertion would not have occurred if OEHHA had undertaken an analysis of the data as part of its scrutinizing of the Springborn reproductive studies. Instead, OEHAA (2001) reported the first POD (a LOAEL of 10 mg/kg/d) for reproductive toxicity of the highly soluble salt of Ni sulphate using erroneous data (i.e., information from Table 17 of the DRF study).

Table A2-1. Perinatal mortality assessment from SLI (2000a).

Dose	Animal #	Implantation scars	Live d0	Dead d0	Dead d0 Average	95% C.I.	Lower 95% C.L.	Upper 95% C.L.
0	192	17	17	0	0.38	0.58	-0.21	0.96
0	196	17	16	1				
0	206	16	16	0				
0	219	13	13	0				
0	221	17	17	0				
0	231	19	17	2				
0	233	16	16	0				
0	237	16	16	0				
10	188	6	6	0	0.71	0.65	0.07	1.36
10	195	17	16	1				
10	224	18	18	0				
10	229	16	0	16[1]				
10	234	14	14	0				
10	236	17	15	2				
10	238	15	14	1				
10	243	18	17	1				
20	177	15	14	1	1.50	1.25	0.25	2.75
20	198	16	15	1				
20	205	16	15	1				
20	208	13	13	0				
20	218	17	12	5				
20	239	16	16	0				
20	241	9	7	2				
20	242	16	14	2				
30	200	17	12	5	2.29	1.69	0.59	3.98
30	204	No impantation data -excluded from analysis						
30	207	14	12	2				
30	212	18	16	2				
30	217	16	15	1				
30	222	15	10	5				
30	230	13	13	0				
30	240	15	14	1				
50	194	15	9	6	3.13	1.69	1.43	4.82
50	199	13	12	1				
50	202	18	16	2				
50	215	16	12	4				
50	216	14	13	1				
50	226	16	12	4				
50	232	16	15	1				
75	197	15	9	6	4.75	1.76	2.99	6.51
75	210	17	14	3				
75	213	15	9	6				
75	220	17	14	3				
75	228	17	12	5				
75	235	12	11	1				
75	244	17	11	6				
75	245	8	0	8				

Footnote 1: Total litter loss was reported for dam 204. Dam 204 has been excluded from analysis.

OEHHA's reporting that 10 mg/kg/d was a LOAEL for perinatal mortality was the first benchmark in a chain of serial regulatory citation, which terminated, for Ontarians, in the Ministry's

"preferred" Ni TRV (MECP, 2019). It was the subsequent definitive Springborn 2-generation reproductive toxicity study (SLI, 2000b), with significantly greater replication, that identified 10 mg/kg/d NSHH (the highest dose group test in the 2-generation study) as the NOAEL for perinatal mortality (SLI, 2000b).

The OEHHA (2005) reference cited by the Ministry stated that OEHHA (2001) "…observed significant pup mortality at the lowest dose (10 mg nickel sulfate hexahydrate/kg-day or equivalent to 2.2 mg nickel/kg-day) and deemed it as the LOAEL for this study."

Furthermore, OEHHA (2005) stated the following:

> Following the range-finding study, Springborn Laboratories (2000b) conducted a two-generation reproduction study. Nickel sulfate hexahydrate was administered at 0, 1, 2.5, 5, or 10 mg/kg-day. Dosing of the F_0 animals began at 10 weeks prior to mating and dosing of the F_1 rats began on postpartum day 22 (just after weaning, at a young age). For both generations, daily dosing of the dams was continued until lactation day 21. In this two-generation study, no adverse effects were observed even at the highest dose, 10 mg/kg-day (2.2 mg nickel/kg-day). In reviewing these three studies in totality, OEHHA concluded that the 1.1 mg nickel/kg/day (5 mg nickel sulfate hexahydrate/kg-day) dose in the two-generation study was the appropriate NOAEL for use in calculating the PHG. It represents the highest NOAEL that is lower than the LOAEL from either the Smith, or Springborn range-finding, study.

In the cited passage, OEHHA (2005) perpetuated the incorrect assertion that the 10 mg NSHH/kg/d dose level in the Springborn DRF study was a LOAEL rather than a NOAEL as was identified by the subsequent 2-generation study (SLI, 2000b). Regardless of the fact that the 10 mg/kg/d "LOAEL" from the DRF study was actually a NOAEL (identified from the 2-generation study), the regulatory approach of the California EPA was to select a POD from the DRF study (SLI, 2000a) rather than using the definitive 2-generation Springborn study (SLI, 2000b) that followed the DRF study. The 2-generation Springborn study (SLI, 2000b) has substantially more replication (28 rats per dose level versus 8 in the range-finding study) and effectively superseded the DRF study with its NOAEL of 30 mg/kg/d. The 2-generation study moved the science forward, but the California regulators selected the less robust POD from the less replicated DRF as the starting point for the derivation of its child-specific reference dose (chRD).

Ontario, in turn, appears to have accepted this work without conducting its own review of the underlying Springborn data. Like many other regulatory agencies, Ontario appears to have also relied, at face value, on the analyses and interpretations of other reputable agencies that, in this case, are clearly and unfortunately incorrect. In conjunction with Vale's previous analysis of Ni TRVs, Vale has clearly demonstrated that the Ministry's "preferred" Ni TRV (of 11 µg/kg bw/day) is not scientifically robust and, in fact, appears to be based on an earlier erroneous data analysis originating with the initial study report from the Springborn DRF.

Vale's presentation on TRV selection mentioned above should be referenced to identify Vale's scientific critique of the other TRV derivations cited as supporting evidence for the Ministry's Ni TRV selection in 2019 (Fig. A2-1), namely Health Canada's TRV adoption from other agencies (HC, 2010) and Cal EPA's 2012 revision of its chRD (OEHAA, 2012).

It is widely understood that the Springborn reproductive toxicity studies of NSHH are the most robust studies in the literature, addressing what is likely the most sensitive toxicological endpoint for NSHH (reproduction – NSHH being previously shown to not be carcinogenic by oral ingestion). The most scientifically robust and transparent derivation of a TRV for NSHH is that of Haber et al. (2017), which used a benchmark dose approach (the Ministry's preferred approach to TRV derivation) and was published in the peer-reviewed literature. Although based on better scientific principles than the much earlier study of Ambrose et al. (1976), conveniently, the numerical value of the Ambrose TRV (20 µg Ni/kg/d) is the same as the Haber et al. (2017) TRV. This value is the most scientifically robust value, is supported by the current state of the science, and is numerically identical to the TRV currently present in Ontario regulation.

Both the DRF study (SLI, 2000a) and the definitive 2-generation study conducted by Springborn Laboratories (SLI, 2000b) administered test animals (rats) with nickel sulfate hexahydrate (NSHH) dissolved in reverse osmosis-deionized (RO-Di) water via oral gavage. Both studies (SLI 2000a,b) provided municipal tap water (treated using reverse osmosis) and Purina Certified Rodent Chow #5002 (Purina Mills, Inc) to all test animals (both controls and test groups). According to SLI (2000a,b), an analysis of the feed and water indicated that, within 'generally accepted limits', there were no contaminants (in the feed or drinking water) that would interfere with the study. More specifically, the definitive 2-generation study (SLI, 2000b), took samples of feed from each new lot and analyzed them via by atomic absorption, most likely flame atomic absorption spectroscopy (FAAS) based on the limits of quantitation (LOQ) reported in Appendix B of SLI (2000b). The analysis indicated that the nickel content in the Purina Rodent Chow #5002 was below the achieved LOQ for NSHH (SLI, 2000b). Appendix B of SLI (2000b) report LOQ values of 20 µg/L and 10 µg/L, depending on the preparation lot number. Based on this information, SLI (2000b) could only have been using FAAS. Literature from Perkin-Elmer report the detection limits for various analytical methods (Table A2-2). In highlighting this, it becomes evident (by the fact that nickel sulfate hexahydrate was not detected above the LOQ achievable using FAAS) that the Springborn studies (SLI 2000a,b) did not consider the dose of Ni received by rats from diet. This is understandable, since Springborn Labs was studying NSHH, not Ni. However, when the results of a NSHH toxicity test are extrapolated in the development of a TRV for human health purposes, baseline dietary Ni from uncontaminated food sources resulting from the natural uptake of Ni from soil into plants and animals (which is a source of dietary Ni not just for the animals used in the toxicity testing, but also for humans for which TRVs are derived) must be considered.

Table A2-2 Reported Detection limits of Various Analytical Methods[a]	
Analytical method	***Detection limit (µg/L)***
Flame atomic absorption spectroscopy (FAAS)	***6***
Graphite furnace (GFAAS)	***0.07***
ICP-OES	***0.5***

ICP-MS	*0.0002*

[a]Perkin-Elmer URL:
https://www.perkinelmer.com/PDFs/downloads/BRO_WorldLeaderAAICPMSICPMS.pdf

Vale conducted in vivo rat studies in 2002 and in 2013 to estimate the bioavailability of nickel in Port Colborne soil (Dutton et al., 2019, 2020). In these studies, the animals had access to food throughout the 4-day studies. In order to estimate the dose of Ni from diet, the concentration of Ni in the rodent chow used in the in vivo experiments was determined (i.e., Harlan Teklad 8728C) as well as the Certified Rodent Chow used in the Springborn studies (Purina lab diet 5002) (Figure A2-2 – Vale Canada Limited – unpublished data). As expected for these diets, which were both sourced from natural ingredients, the values were comparable and indicate that the concentration of nickel in the Purina Certified Rodent Chow used in the Springborn (2000a,b) studies was certainly measurable when using appropriate analytical methods, and was found to contain 1.45±0.1 µg Ni/g food (95% C.I. 0.16 µg Ni/g).

Purina certified 5002 diet ingredients (used in SLI (2000a,b)	*Harlan Teklad certified rodent diet 8728C ingredients (used in Dutton et al. (2019)*
Ni concentration in the diet: 1.45 µg Ni/g food (95% C.I.) [1.29, 1.61]	**Ni concentration in the diet: 1.94 µg Ni/g food (95% C.I.) [1.53, 2.35]**
Sources of Ni in the diet: **Ground corn, dehulled soybean meal, ground wheat, fish meal, wheat middlings, brewers dried yeast, cane molasses, wheat germ, dried beet pulp, dehydrated alfalfa meal, ground oats, soybean oil, dried whey, ground soybean hulls,**	**Sources of Ni in the diet:** **Dehulled soybean meal, wheat middlings, flaked corn, ground corn, fish meal, cane molasses, ground wheat, dried whey, soybean oil, brewers dried yeast**
Other dietary components: calcium carbonate, casein, salt, choline chloride, DL-methionine, cholecalciferol, menadione dimethylpyrimidinol, bisulfite (vitamin K), vitamin A acetate, dicalcium phosphate, folic acid, thiamin mononitrate, vitamin B12 supplement, nicotinic acid, calcium pantothenate, riboflavin, manganous oxide, zinc oxide, ferrous carbonate, copper sulfate, zinc sulfate, calcium iodate, cobalt carbonate, sodium selenite.	Other dietary components: dicalcium phosphate, calcium carbonate, iodized salt, choline chloride, kaolin, magnesium oxide, ferrous sulfate, vitamin E acetate, menadione sodium bisulfite complex (source of vitamin K activity), manganous oxide, copper sulfate, zinc oxide, niacin, thiamin mononitrate, vitamin A acetate, vitamin D3 supplement, calcium pantothenate, pyridoxine hydrochloride, riboflavin, vitamin B12 supplement, calcium iodate, folic acid, biotin, cobalt carbonate.

Fig. A2-2. Composition of rat chow diet used in Springborn (2000a,b) (Purina certified 5002) and in Dutton et al. (2019) (Harlan Teklad 8728C)

The contribution of Ni from diet alone is significant and cannot be overlooked. Control animals in the SLI (2000a,b) studies[9] were receiving approximately 70 µg/kg/d to 175 µg/kg/day Ni from food alone (Figure A2-3). This represents approximately 3% to 8% of the NOAEL (2,200 µg Ni/kg/d) for oral administration of NSHH over two generations of rats (SLI, 2000b) and 6% to 16% of the inappropriate POD (1,100 µg Ni/kg/d) that was rationalized and adopted for use by DEPA 2008), OEHHA (2012) and HC (2010).

[9] Male rats have been considered in this analysis, but the trends are similar for females, although female rats are typically smaller than male rats at a given age and consume less food per unit body weight.

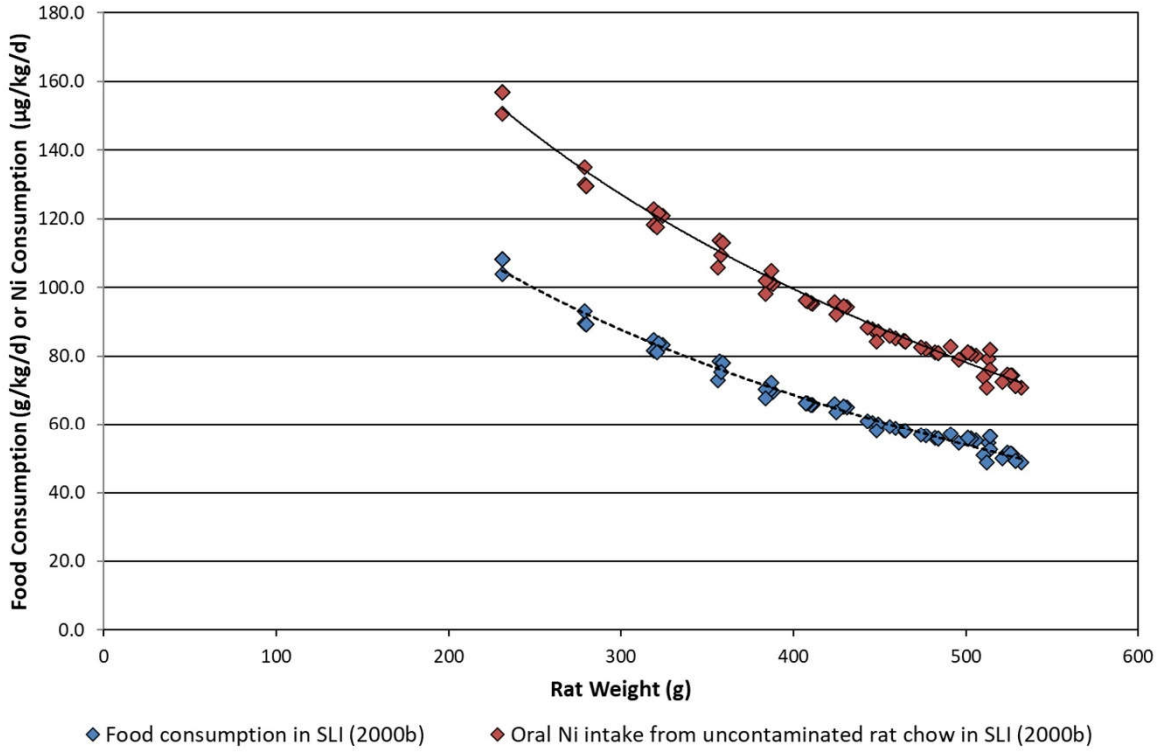

Fig. A2-3. Body-size-dependent food consumption and associated baseline Ni consumption from male rats from Springborn (2000a,b). Rats were fed Purina certified 5002 diet containing 1.45 µg Ni/g food (95% C.I.) [1.29, 1.61]. The NOAEL dose from Springborn (2000b) is 2,200 µg Ni/kg body weight/day. Rats can consume between 3 and 7% of the NOAEL dose just from uncontaminated food. This has not been considered in TRV derivation until now.

As part of a review of the toxicology of soluble nickel compounds prepared by the Toxicology Excellence for Risk Assessment (TERA, 1999), an oral reference dose of 8 µg Ni/kg/d for ingested nickel-soluble salts was derived. TERA (1999) derived its oral RfD using data generated by Vyskocil et al. (1994), where male and female rats showed an increase in albuminuria (an indication of renal glomerular dysfunction) after being exposed to nickel in drinking water for 6 months. A minimal study LOAEL of 7.6 mg Ni/kg/d was identified and a composite uncertainty factor (UF) of 1,000 (10 for human variability, 10 for inter-species variability, and 10 to account for sub-chronic-to-chronic extrapolation, an insufficient database, and the use of a minimal LOAEL) was applied to derive an oral RfD of 8 µg Ni/kg/d. TERA (1999) clearly indicates that the nickel doses cited in the animal study (used to derive the oral RfD) did not include nickel exposure from the diet and, therefore, the oral RfD (of 8 µg Ni/kg/d) represents the dose of nickel <u>in addition</u> to the amount obtained from food.

The oral RfD (of 8 µg Ni/kg/d) was considered, by TERA (1999), to be consistent with the oral RfD developed by the US EPA (of 20 µg Ni/kg/d) based on Ambrose et al. (1976). The rationale provided was that a) the US EPA oral RfD was based on total Ni intake (including diet) while TERA's oral RfD (of 8 µg Ni/kg/d) was in addition to diet and as such, TERA's RfD was expected to be lower than that of the US EPA; and b) TERA's oral RfD (of 8 µg Ni/kg/d) was within a factor of

2 of the US EPA's RfD value, a difference considered by TERA (1999) to be within the range of uncertainty surrounding the RfD. Although an independent peer review panel, through TERA's Peer Review program, approved the RfD, TERA's oral RfD (of 8 µg Ni/kg/d) was not used in the Sudbury Area Risk Assessment (SARA) as the oral RfD values for all other chemicals of concern were expressed on a total exposure basis. The TERA's oral RfD was considered an incremental value or to be in addition to dietary sources (SARA, 2008). As with the TERA (1999) oral RfD (of 8 µg Ni/kg/d), any TRV developed using the Springborn data (SLI, 2000a,b) needs to be interpreted in addition to the Ni obtained from baseline dietary sources.

Failure to recognize the significance of baseline dietary Ni intakes in the Springborn studies (SLI, 2000a,b) and others, such as Vyskocil et al. (1994), has a direct implication on how the TRV should be applied. By way of example, default uncertainty factors (UFs) for inter-species variability (a factor of 10) and human variability (a factor of 10) applied to an inferred NOAEL of 1,100 µg Ni/kg/d (rationalized by OEHHA (2012), HC (2010), DEPA (2008) and others), results in a TRV (11 µg Ni/kg/d) that is essentially equal to the average daily dose received by young children (1 to 4 years of age) as a result of consuming a typical Canadian diet.

Health Canada's Total Diet Survey reports a range of average dietary Ni intake rates (on a µg Ni/kg/d basis) for different age groups, including young children between the ages of 1 and 4 years, the primary group of interest as it pertains to Ni exposure from soil and dust. Between the years 2000 and 2007 Health Canada reported average dietary Ni intake rates of between 5.5 µg Ni/kg/d to 18.6 µg Ni/kg/d for male and female children combined (1 to 4 years), with an average dietary intake (over the 8 year period from 2000 to 2007) of 11.1 µg Ni/kg/d (Table A2-3 and Fig. A2-3). The current approach, which fails to accommodate baseline dietary Ni exposure, makes it appear that the entire Canadian toddler population is at risk of Ni toxicity, which is clearly incorrect (Fig. A2-4 and Fig. A2-5). Consistent with the interpretation and application of the TERA (1999) TRV (of 8 µg Ni/kg/d), any TRV developed using SLI (2000a,b) regardless of its value, should be applied in addition to baseline dietary exposure.

Table A2-3 Average Dietary Intakes (µg/kg/d) of Nickel in Canada from 2000 – 2007[a]		
Year	*City*	*Average Dietary Intake (µg/kg/day) – M&F Children (1 to 4 years)*
2000	*Ottawa*	*18.62*
2001	*St John's*	*15.01*
2002	*Vancouver*	*14.75*
2003	*Montreal*	*9.2*
2004	*Winnipeg*	*8.7*
2005	*Toronto*	*7.4*
2006	*Halifax*	*5.5*
2007	*Vancouver*	*9.8*
Average (2000 – 2007)		*11.1*

[a]Health Canada – Canadian Total Diet Survey https://www.canada.ca/en/health-canada/services/food-nutrition/food-nutrition-surveillance/canadian-total-diet-study/dietary-

intakes-contaminants-other-chemicals-different-sex-groups-canadians.html

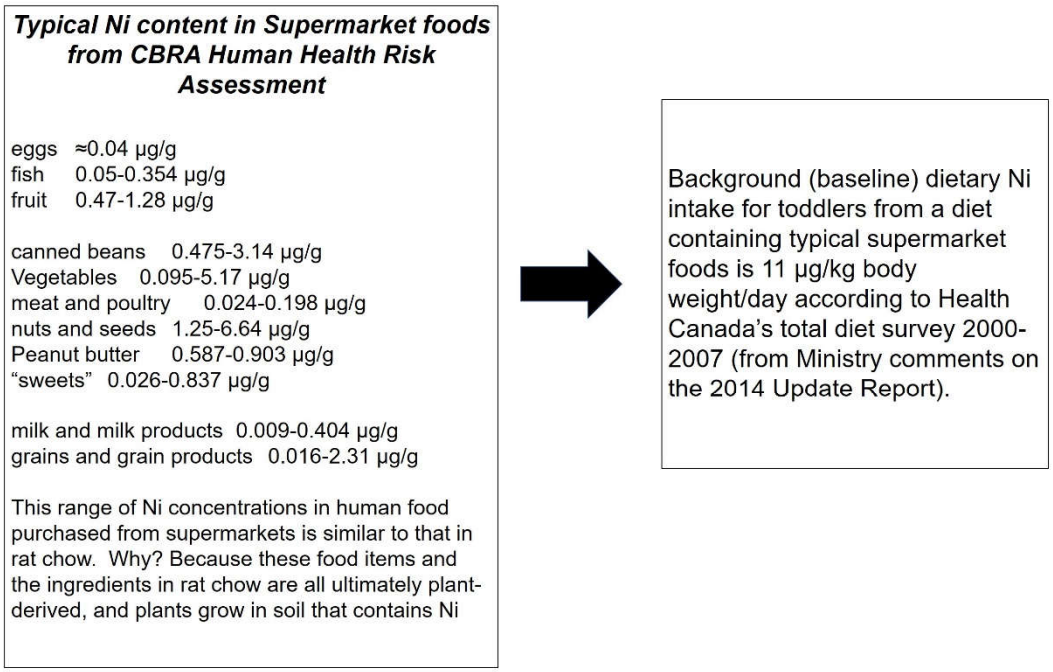

Fig. A2-4. Baseline Ni concentrations (fresh weight basis) in supermarket food items analyzed as part of the CBRA HHRA.

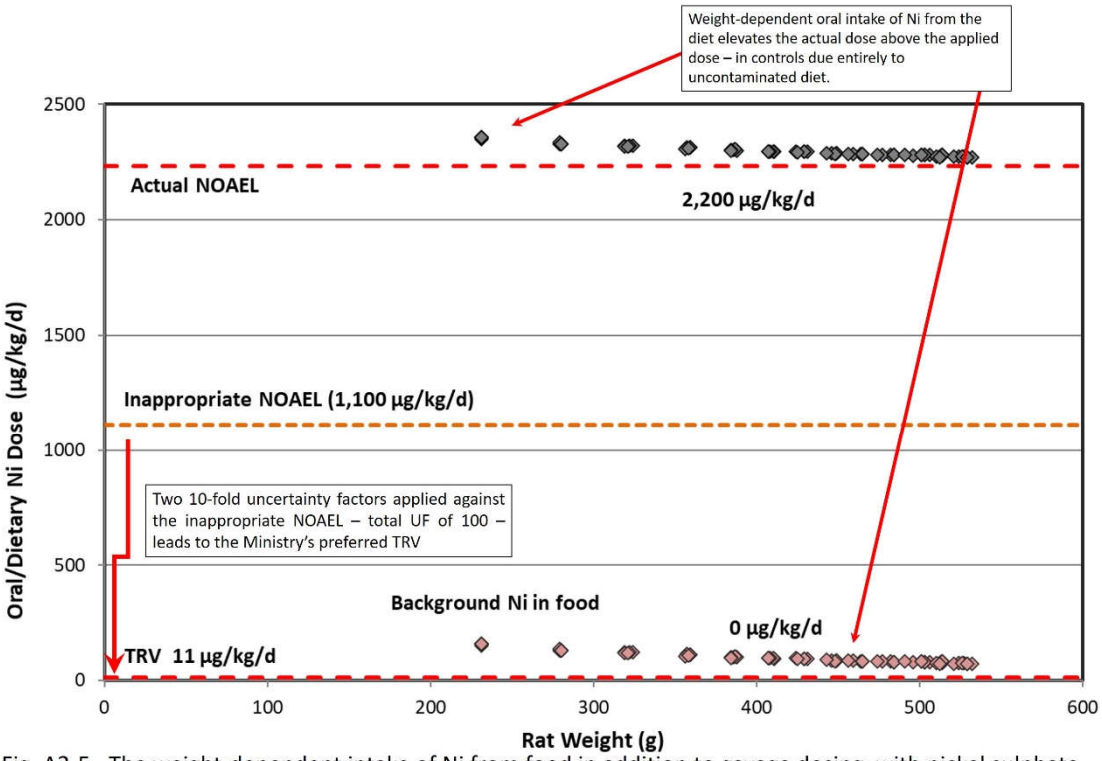

Fig. A2-5. The weight-dependent intake of Ni from food in addition to gavage dosing with nickel sulphate hexahydrate in F0 male rats from the Springborn study raises the actual dose above the measured doses. Use of 100-fold UFs results in the TRV for humans being at the baseline exposure level for uncontaminated food.

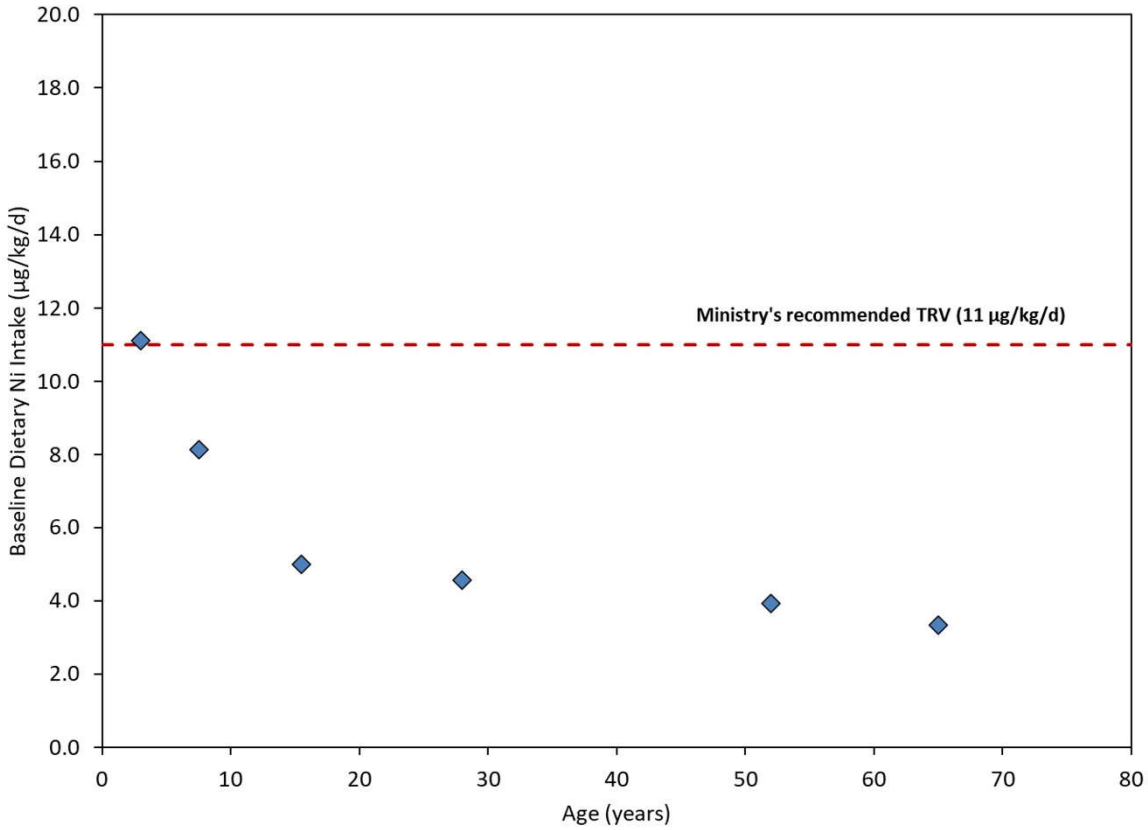

Fig. A2-6. The human age-dependent baseline intake of Ni from uncontaminated food in Canadians cities between 2000-2007. Data from the Canadian Total Diet Survey. Age groups were 1-4 years, 5-11 years, 12-19 years, 20-39 years, 40-64 years, and 65+ years. Values are the averages for males and females jointly. Approximate mid-points of the age groups are plotted. Use of 100-fold UFs, applied to an inappropriate NOAEL results in the TRV for humans being at the baseline exposure level for uncontaminated food.

<u>European Food Safety Authority (2020)</u>

EFSA (the European Food Safety Authority) released a TDI (tolerable daily intake) value of 2.8 µg/kg body weight/day in 2015. The EFSA TDI used a benchmark dose (BMD) approach and was quite flawed, as previously presented to the Ministry by Vale. In 2017, Haber et al. (2017) published a peer-reviewed BMD reassessment of the Springborn data. The Haber et al. (2017) study was open and transparent and provided their data so that others could replicate their calculations if desired. Haber et al. (2017) used the BMD approach and proper metrics describing post-implantation and perinatal loss (PPL), ultimately deriving a TRV of 20 µg/kg body weight/day. Haber also provided a critique of the EFSA (2015) derivation.

The European Commission required EFSA to revise its 2015 TDI (of 2.8 µg/kg body weight/day). EFSA has recently released a revised TDI value in draft, which is now 13 µg/kg body weight/day (EFSA, 2020). The revised TDI still lacks transparency regarding its derivation. Consequently, the Haber et al. derivation is still preferred over the opaque supporting documentation currently provided by EFSA which does not allow an independent scientist to scrutinize EFSA's derivation.

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Annex 3 Vale's Interpretation of Bioavailability of Port Colborne Soils.

The Ministry has provided detailed comments on the aspect of bioavailability and bioaccessibility adjustments for both the ecological and human risk assessments. When the CBRA was initiated, the use of bioavailability adjustments in risk assessment was a relatively new phenomenon, but was known by the majority of practitioners to be important and necessary. At the time, it was generally recognized that by not including such adjustments, risk estimates resulting from exposures of individuals to certain metals in soil and/or dust could be highly inflated in many cases.

Bioaccessibility (BAc) and bioavailability (BAv) have undergone significant discussion in the CBRA, and the reader is referred to the original CBRA documents and the 2014 Update Report for background. Briefly, BAc is an indirect estimate of BAv and is determined in vitro, whereas BAv is determined using live organisms. BAc provides conservative estimates of true BAv because it only considers the dissolution (leaching) of target substances (here, Ni, Cu, Co, and As) from the soil matrix. BAc measurements ignore the components of BAv that relate to competitive uptake (both in terms of diffusive transport across cell membranes and facilitated uptake and active transport across membranes). The most conservative approaches for estimating BAc use acidic assay conditions that mimic the acid conditions of the stomach (usually pH 1.5), thereby maximizing the dissolution of metals from the soil matrix. For metals and metalloids that are absorbed via the intestinal epithelium, some methods adjust the pH upwards to intestinal pH (ca. pH 7.5) at which point the solubility of Ni and other cationic metals is reduced relative to lower pH. This pH adjustment typically results in reduced estimates of BAc.

The chemical form (speciation) of metals in soil affects both BAv and BAc. Highly soluble salts of Ni are highly bioaccessible, and although poorly bioavailable in an absolute sense, they (soluble salts) are the most bioavailable form of Ni. In a recent publication concerning the in vivo bioavailability studies conducted using Port Colborne soils, rats were gavage dosed with $NiSO_4 \cdot H_2O$ at the same dose levels used in the Springborn 2-generation reproductive study to mimic the BAv that would have been occurring during the Springborn studies (Dutton et al., 2019). The absolute BAv of Ni from $NiSO_4 \cdot H_2O$ was found to be approximately 2%. Elsewhere, the BAc of $NiSO_4 \cdot H_2O$ (NSHH) has been estimated by others to be approximately 92% (Henderson et al., 2012; Lau, 2012), showing the large degree of conservatism that exists between BAv and BAc for this highly soluble Ni salt. In contrast, the fill, clay, and organic soils displayed a range of BAc values and much lower BAv; relationships between BAc and BAv were developed that highlight these differences (Dutton et al., 2019). The Ni, Cu, and Co in the contaminated soils near Port Colborne are present in poorly bioavailable forms, as previously documented in the CBRA and more recently described in Dutton et al. (2019).

The Ministry provided the following comments on bioavailability correction in its memo of September 27, 2007, in which it reviewed the draft CBRA HHRA.

"The Ministry's position is that SARA can use currently acceptable methods to adjust soil and dust CoC intakes as follows:

(A) using RAF (soil-oral) based directly on the measured in vitro bioaccessibility results (this approach assumes that the TRV is 100% bio-available and the bioaccessibility data is the upper estimate of bioavailability):

• CoC intake from soil or dust = Soil ingestion rate (SIR) X CoC soil concentration X bioaccessibility value, or

(B) a relative bioaccessibility based RAF (soil-oral) which is based on the measured in vitro bioaccessibility of the soil or dust and the reported or estimated bioaccessibility of the medium in the TRV:

• CoC intake from soil or dust = SIR X CoC soil concentration X (bioaccessibility of CoC in soil / bioaccessibility of CoC in TRV medium), or

(C) using RAF (soil-oral) based on the relative bioavailability (RBA) of the soil CoC and the bioavailability of the CoC in the TRV medium:

• CoC intake from soil or dust = SIR X CoC soil concentration X (absolute bioavailability of CoC in soil / absolute bioavailability of CoC in TRV medium).

MOE (and USEPA) already permit the use of methods A and C. Method B combines A and C, but does not appear to be used extensively at this time. In all cases, a proponent should support their calculations with relevant science from the literature and supporting data from speciation, as well as other studies pertaining to the solubility and/or bio-availability of the CoC in question MOE further comments on the SARA data for the in vitro bio-accessibility of lead in Sudbury soils in terms of measurement reliability, QA/QC and whether it meets required analytical sensitivity criteria (± 20 to 25%). Also, the sequential extraction results and the speciation data in the Sudbury study appear to validate the in vitro data.

Further examination of the scientific literature regarding upper limits on the bioavailability of soluble lead may assist SARA in applying methods A, B or C."

With regard to data for in vitro bio-accessibility, the consultant should ensure measurement reliability, QA/QC and whether it meets required analytical sensitivity criteria (± 20 to 25%). Also, the sequential extraction results and the speciation data in should be reviewed to validate the in vitro data.

<u>Later comment (part of MOE's response to the proponent (September 6, 2007))</u>

The issue for CoCs other than lead is that USEPA does not officially consider use of in vitro bioaccessibility values without the requisite level of in vivo validation as credible. Arsenic is in the position of having considerable in vivo validation (the State of Hawaii has promulgated soil standards for bioaccessible arsenic *http://www.hawaii.gov/health/environmental/hazard/pdf/arsenicactionlevelsaug2006.pdf).* However, USEPA has only validated the use of IVBA for lead http://epa.gov/superfund/bioavailability/guidance.htm, July 3, 2007). USEPA has recently proposed a Recommended Decision Framework for Assessing Oral Bioavailability (BA) of Metals at Contaminated Sites (see url above). USEPA has instituted a special committee to validate bioavailability assessments. For a proponent to use in vivo or in vitro based data to adjust bioavailability for non-validated CoCs, the default is to use 100% bioavailability. If this 100% approach results in an exposure calculation that exceeds the TRV being used then any proposed bioavailability adjustments must be supported by strong weight of evidence arguments. MOE recommends that proponents contact SDB for advice.

BAc and BAv analyses have been conducted for Port Colborne soils. The Ministry has conducted BAc on fill soils from the Rodney Street community, and within the initial CBRA HHRA, BAc and BAv were conducted on only three samples, one each of a fill, a clay, and an organic soil. This level of coverage of the soil types was insufficient to characterize the BAv and BAc of these soils. Vale conducted additional BAv studies to increase the sample coverage, gavage dosing male Sprague-Dawley rats with soil solutions in methyl cellulose carrier. The Ministry has previously commented that because several of these samples were from the same location, there is less coverage than it might appear, and that this invalidates the BAv data. Despite these shortcomings, the BAv study conducted for the 2014 CBRA Update Report has been published in the peer-reviewed literature (Dutton et al., 2019) and has contributed substantially to the BAv weight of evidence for the contaminated Port Colborne soils.

The BAv studies conducted for the CBRA evaluated the availability of NSHH. As mentioned above, the initial BAv study evaluated $NiSO_4 \cdot H_2O$ taken up into blood and excreted in urine, while the Update BAv study evaluated $NiSO_4 \cdot H_2O$ BAv only via urinary excretion mass balance (Dutton et al., 2019). The Ministry has commented previously that single oral gavage doses are inappropriate because they do not represent steady-state conditions. In fact, single oral doses represent the best way to get an accurate estimate of oral bioavailability because the approach gives unambiguous evidence of true bioavailability. Fig. A3-1 provides an example of such evidence, from the CBRA HHRA.

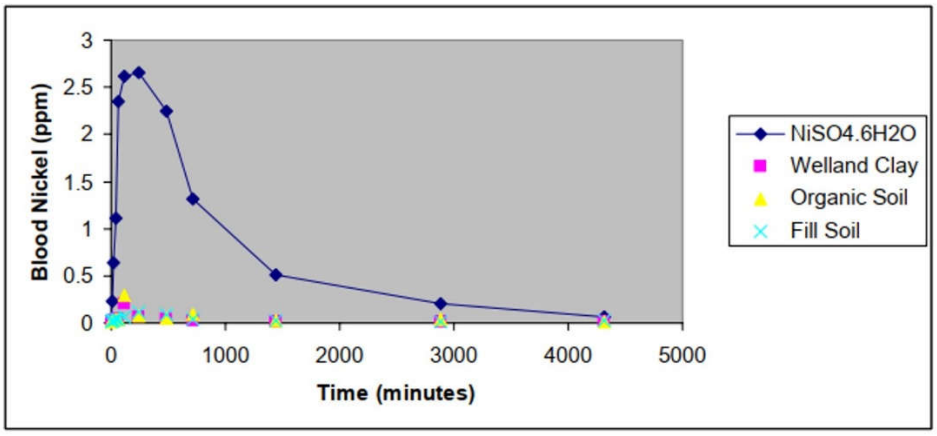

Fig. A3-1. Blood Ni concentrations following single gavage dosing with Ni-containing soil and $NiSO_4 \cdot H_2O$. The figure was originally Fig. 6 on PDF page 740/1187 (p. 33) of Appendix 8 of "Volume III: Exposure Calculations and Toxicity" dated December, 2007. This can also be found in Appendix 1M of the 2014 Update Report.

Single oral dose studies are the preferred approach to estimating oral Ni BAv.

The Ministry has previously stated that it considers only juvenile swine studies to be acceptable sources of evidence of bioavailability. However, based on item "C" in the Ministry's statements above, the most logical approach (given that the TRV is based on a rat toxicity study) is to conduct the bioavailability study of site soils using rats, not juvenile swine.

The discussion above has focused on the oral bioavailability of Ni from incidentally ingested soil. The oral bioavailability of Ni and the other CoCs from food in the CBRA to date has assumed that the bioavailability of Ni present in food items is 100% - i.e. all Ni ingested in food will be systemically available to cause toxicity. In the Update Report, BAv studies found that the baseline dietary Ni bioavailability in rats fed a naturally sourced diet containing 1.94 mg Ni/kg was approximately 2%, not 100% and the BAv of Ni in gut-cleared worms was 6.87% 95% C.I. [2.27,11.48] (the upper confidence limit value was used in the ecological risk calculations in Annex A1). Failure to incorporate realistic BAv estimates for baseline dietary Ni consumption greatly inflates risk estimates. The literature on the BAv of baseline uncontaminated Ni exposure is developing. Recently, Babaahmadifooladi et al. (2020) reported BAc and BAv estimates from dietary items and found that using an assumption of 100% BAv will overestimate the true exposure.

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Annex 4 Additional Figures Requested by the Ministry

(See pdf attachments)

Annex 5 Comment-Response Dialogue associated with Ministry-Vale Discussion of Male Reproductive Effects.

(See pdf attachment)