Guidance on Human Health Risk Assessment

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northern health
the northern way of caring

Evaluation of Risks

While environmental quality guidance values (e.g., air quality criteria, drinking water guidelines, soil guidelines, etc.) provide a basis for protecting the general population from adverse effects of environmental pollutants, it is not sufficient to limit the question to: "Are the public exposures below the health criteria?" Compliance with current limits is not sufficient. Most chemicals have no health (exposure) limits. For the chemicals that do have existing health limits, the information used to set limit may be incomplete, or out of date. Existing limits are not always designed to protect the most sensitive people. Further, each day, new toxicological and epidemiological information are gathered, and new exposure limits will be generated for environmental agents, i.e.,

- New exposure limits for environmental agents that formerly had none.
- Changes to the existing exposure limits for some environmental agents. Usually, if there is a change to the health limit, that benchmark value is re-adjusted (usually lowered).

Further, short-term excess does not necessarily mean that adverse effects automatically occur (Berglund, Elinder, and Järup, 2001); that exceedance (data) should be evaluated based on the relative increase in risk of adverse health effect(s).

It is important to stress that, as part of the health risk assessment (or study), exposures are characterized well enough, and other risks that are presented by that exposure are considered (and assessed). The goal is to ensure that the present health risks are within acceptable limits, and future risks are (or can be) reasonably managed. Hence, health exposure evaluation extends beyond today's state and into the future, as well.

Literature Search

As part of the HHRA process, a literature search is performed to gather the necessary information to gain any understanding of what is known (or unknown) about an environmental agent, and its (potential) health effect(s).

When reviewing the evidence that is presented in the scientific research papers, it is important to evaluate that evidence based on, for example, the type of study, data collection (or monitoring) methodology, sample size and statistical method used to interpret the data, control for confounders, strength (and consistency) of association (of dose-response, biologic plausibility), etc.

Four Main Stages of HHRA

The aim of human health risk assessment is to identify and quantify past, present, and future exposures to environmental (chemical, physical, or biological) agents that may cause health effects (Berglund, Elinder, and Järup, 2001). The methods and assumptions used in the HHRA process should ensure that the "human exposures and potential risk for adverse human health effects are not underestimated".

Generally, the HHRA study comprises of four main stages (Hopkins and Williams, 2011): problem formulation, toxicity (or hazard) assessment, exposure assessment, and risk characterization (see Figure 1).

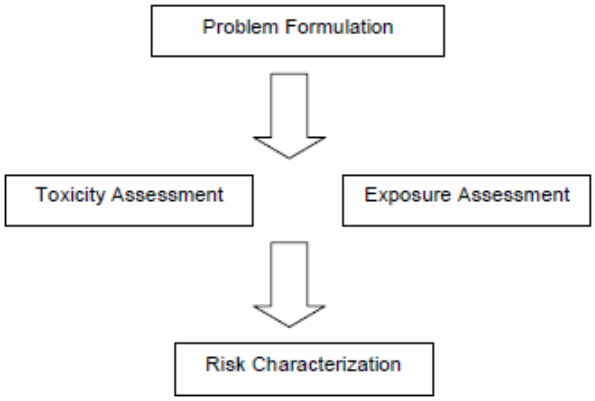

Figure 1. HHRA Framework (Hopkins and Williams, 2011).

The following steps will provide a general guidance in the completion of a health impact or risk assessment review (or study).

1. Problem Formulation

The objective of the 'problem formulation' stage is to prepare a (or assess the) conceptual site model (CSM) that describes the possible contaminant source influences that may be present, and the possible linkages between source-pathway-receptor.[1] The CSM should adequately describe in the text and illustrated by appropriate plans, drawings, etc, the following components:

- site condition(s);
- hazard identification, i.e.,
  - all the chemicals/contaminants that are present, emitted, or discharged, and
  - all potential sources of the contaminant(s);
- all potential migration and exposure pathways; [2]
- all potential receptors and the sensitivity of the study area; and
- a clear graphical presentation of the conceptual model.

The complexity and level of effort for the HHRA review will depend on the contaminant source, exposure pathway, and receptor combinations (Hopkins and Williams, 2011).[3]

A profile of baseline conditions (e.g., baseline health status or environmental conditions) should be included as part of the outcome assessment. Baseline 'health status' conditions should include documentation of both population health vulnerabilities (based on the population characteristics), and equalities in health outcomes among subpopulations or places (Bhatia et al, 2009).

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[1] Input from the affected community stakeholders, local authorities or decision makers (e.g., hamlet, village, or municipal government), and individuals or organizations knowledgeable about or responsible for the health of the community (e.g., community health center, health care providers) should be considered in the development of the CSM.

[2] The HHRA process should include consideration of all potential pathways that could reasonably link the proposed activity, or product or technology use to health, whether direct, indirect, or cumulative.

[3] For example, inhalation exposure to chemicals in the air may be evaluated by comparison of (modeled or measured) air concentrations with published health criteria. Food consumption, on the other hand, may require more complex and multi-media exposure modeling (Hopkins and Williams, 2011).

1.1 Study Boundaries

In defining the CSM, study boundaries may be defined, i.e.:

- **Spatial Areas** (local or regional) – Adequate definition of the study area boundaries is critical to the identification of human receptors for the HHRA.

  Local study area boundaries may be derived from "the anticipated spatial distribution of potential impacts based on the specific release, transport, and exposure mechanisms" (Hopkins and Williams, 2011).

- **Temporal** – For HHRA, **temporal** considerations would include acute, sub-chronic, and chronic exposures, i.e., the exposure duration and timeframes over which the potential health risks may be exhibited. It is important that the relevant exposure limit (or toxicity benchmark) is consistent with the study exposure averaging time; otherwise, suitable factors are applied for extrapolating between averaging times (Hopkins and Williams, 2011). The 'averaging time' used in the HHRA study should be rationale and relevant to that case scenario (health concern).

In the absence of toxicity benchmarks for short-term (acute or sub-chronic) exposure periods, short-term exposures may be compared with longer term exposure limits to ensure that risks are not underestimated (Hopkins and Williams, 2011).

To ensure that the human health risks are adequately assessed, both the spatial and temporal boundaries must be appropriate and applicable to the case file.

1.2 Identification of Receptors

As part of the HHRA process, the potential adverse health effects or impacts on the receptor (individual, community, or population) must be assessed. The information on the receptor characterizations (age classes[4], vulnerable groups, lifestyle and behavioral characteristics, physical & medical conditions, land use[5]), and locations (and local land use designations) are identified in the CSM. Depending on the exposure pathways, an HHRA study may be conducted for all receptor locations, or just those identified as critical (Hopkins and Williams, 2011).

The US EPA (2006) has recommended that factors specific to exposure assessment for children should be addressed (separately from adults) whenever it appears that their risks might be greater than those of adults. The reasons for that such special treatment are as follows (US EPA, 2006):

- **Children** may be **more** exposed to the environmental toxicants than adults.
- **They** consume **more** of certain foods and water per pound of body weight than adults.
- **Children** have higher inhalation rates per pound of body weight than adults.
- **Young children** play close to the ground, and come into contact with contaminated soil outdoors and surface dusts.
- **Exposure** to chemicals in breast milk affects both infants and young children.

Thus, US EPA has provided the Child-Specific Exposure Factors Handbook as a reference guide for children's exposure assessment.

[4] infant, toddler, child, and adult

[5] This pertains to residential, agricultural, commercial, industrial, institutional, recreational, or areas that are subject to Aboriginal and other traditional land use.

1.3 Exposure Pathway Identification

Potential exposure pathways for all chemicals of potential concern and receptors should be identified in the HHRA study. The exposure pathway encompasses consideration of the chemical/contaminant source, mechanism of the chemical/contaminant release, transport mechanism in the relevant media, receptor, and exposure route (or mechanism of intake) (Hopkins and Williams, 2011), e.g.:

- inhalation of volatile contaminant or particulate matter;
- ingestion of contaminants in the water, soil, or food (produce, vegetation, fish, game, etc.); and
- dermal contact with contaminants in the soil or water.

2. Exposure Assessment

2.1 Exposure Assessment

Exposure assessment is "crucial for the identification, evaluation, and control of health risks in the general environment. For environmental agents that have existing health limits or criteria, the "basis for control of health risks is guidelines and standards" (Berglund, Elinder, and Järup, 2001). An exposure assessment may involve an estimation of the exposure intensity (based on environmental sampling, fate and transport modelling, dose calculations, etc), and how it varies over time for the exposure group(s), route of exposure, etc. In some cases, there may be a lack of quantitative data, so exposure profiles will be based on qualitative information.

2.2 Toxicity Assessment

Depending on the potential exposure pathways and scenarios in play, the health risk assessment must always consider both 'toxicity-based', and 'persistence and bioaccumulation-based' criteria, in addition to the route of exposure (or exposure pathway), duration, and receptors.

3. Toxicity-Based Screening Level Risk Assessment

Health effects that can be assessed quantitatively are compared to published exposure limits[6]. The interpretation of that benchmark depends on the nature of the chemical and its mode of toxicity (Hopkins and Williams, 2011). The toxicity information (or screening levels) used in quantitative health risk assessment may come from the following sources (examples):

- **BC Ambient Air Quality Objectives** (http://www.bcairquality.ca/reports/pdfs/aqotable.pdf)
- **Health Canada** Toxicity Reference Values and Chemical-Specific Factors (http://www.hc-sc.gc.ca/ewh-semt/pubs/contamsite/part-partie_ii/index_e.html)
- **US Environmental Protection Agency** Integrated Risk Information System (IRIS) (http://www.epa.gov/iris)
- **California Environmental Protection Agency** (http://www.oehha.ca.gov/risk/ChemicalDB/index.asp)

[6] Exposure limits are also referred to as health 'criteria value' or 'benchmark'.

- **Agency for Toxic Substances and Disease Registry** Minimal Risk Levels (MRLs) (http://www.atsdr.cdc.gov/mrls/index.html)
- **World Health Organization** (http://www.euro.who.int/air)
- **Texas Commission on Environmental Quality** Air Monitoring Comparison Values (AMCV) (http://www.tceq.texas.gov/toxicology/AirToxics.html)
- **Netherlands National Institute of Public Health and the Environment** (RIVM) (http://www.rivm.nl/en/)

In quantitative risk assessments, exposure limits are expressed separately for the chemical class (carcinogens versus non-carcinogens), and route of exposure.

3.1 Non-Carcinogens

Non-carcinogens exhibit a threshold dose, i.e., an exposure limit to which a receptor can be exposed over a long period of time without risk of an adverse health effect. Such exposure limits are expressed as reference concentrations (RfC) for air (or inhalation) exposures, and reference doses (e.g., TDI, RfD) for exposures to other media (other than air) (Hopkins and Williams, 2011).

Ideally, the total exposure of an individual to a non-carcinogenic chemical should not exceed that threshold dose. If the dose is exceeded, then the potential for an adverse effect should be further evaluated.

3.2 Carcinogens (DNA-Reactive or Genotoxic)

Genotoxic carcinogens are considered to exhibit non-threshold effects. The potency of carcinogens is typically expressed as a slope factor (SF), or as a unit risk factor (UR). The UR is calculated from SF, which represents the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent. It should be emphasized that, unlike RfCs, URs do not represent 'safe' exposure levels; rather, they describe the relationship between the level of exposure and the probability of effect or risk. With the exception of epi-genetic carcinogenic chemicals,[7] carcinogens are considered to pose a 'non-zero' risk of cancer at any level of exposure; the risk of cancer will increase with increased degree of exposure. For the purpose of assessing carcinogens, Health Canada, Alberta Health and Wellness, Alberta Environment and Sustainable Resource Development, and Alberta Health Services consider the acceptable incremental lifetime cancer risks (ILCR) to be one-in-hundred thousand (1.0×10^{-5}) per environmental medium for each carcinogen.

Both the UR and ILCR can be used to calculate the toxicological reference value (TRV) for carcinogens. The carcinogenic TRV can be derived by dividing the ILCR by the UR value (see Equation 1). The TRV is the concentration or dose at which the cancer risk considered acceptable, tolerable, or essentially negligible.

Equation 1 $TRV_{carcinogenic} = ILCR \div UR$

It should be noted that tolerable cancer risk level of "1.0×10^{-5}" was developed to address cancer risks that are above background.[8]

[7] Epi-genetic (nongenotoxic) carcinogens do not attack DNA; their actions do not subsequently lead to genetic alteration. For these carcinogens, the principle of threshold dose can be applied. The cancer mechanism is not considered to be operative at exposures below that threshold value (Hopkins and Williams, 2011). Examples of nongenotoxic carcinogens include chlorinated compounds (carbon tetrachloride, chloroform); organochlorine pesticides (dieldrin, DDT, chlordane); peroxisome proliferators (DEHP, clofibrate, nafenopin); organochlorine compounds (TCDD, PCBs), hormones (estradiol, diethylstibestrol); and barbiturates (phenobarbital, sodium barbital) (Kaunig, Kamendulis, and Xu, 2014; Rakitsky, Koblyakov, and Turusov, 2000).

[8] Therefore, for background concentrations, it is recommended that a separate ILCR calculation be completed.

3.3 Persistence and Bioaccumulation-Based Consideration

Consideration of the fate and persistence of a chemical is important, especially, if there is a potential for human exposure to (or uptake of) that chemical via a secondary media. For example, polycyclic aromatic hydrocarbons (PAHs) are known for their persistence and potential for bioaccumulation. For chemicals, like PAHs, the half-life in soil, octanol-water partitioning coefficient (K_{ow}), and other physical-chemical properties should be applied in assessing the persistence and potential for bioaccumulation of that chemical.

3.4 Cumulative Risk Assessment

The US EPA (2003) emphasized that it is important to

- understand the accumulation of risks from multiple environmental stressors or agents,
- recognize the possibility of synergistic interactions and potential risks from aggregate exposures to multiple stressors or agents, and
- consider 'extreme variability among individuals' in their responses to toxic substances.

For clarity, the definition of 'stressors (or agents)' is not limited to chemical contaminants. Stressors can be biological or physical agents, or an activity that can negatively impact health. Further, risks from multiple agents or stressors need not be combined (i.e., added), but rather, an analysis is conducted to determine how the risks from the various 'agents or stressors' interact. The US EPA publications provide guidance on approaches and methods for cumulative risk assessment methods (see http://www.epa.gov/raf/publications/guidelines-for-hra-chemical-mixtures.htm, and http://www.epa.gov/ncer/cra/).

4. Risk Characterization

A judgment is made about the exposure to an environmental agent, using the exposure profile and information collected on the agent's toxicity (see Figure 2).

There are three possible judgment outcomes (Mulhausen and Damiano, 2006):

- **Unacceptable exposures – Implement Health Hazard Controls** The implementation of mitigation measures (or controls are recommended for exposures that are judged as unacceptable. For scenarios involving multiple environmental agents that are contributing to that unacceptable exposure, higher exposures to higher toxicity agents should be controlled first.
- **Uncertain Exposures – Collect Additional Information** Further risk characterization or additional information gathering are recommended for exposures that not well understood, or for which acceptability judgments cannot be made with high confidence.[9]
- **Acceptable Exposures – No Action or Define a Routine Monitoring Program** Until it is time for a reassessment, exposures that are judged as acceptable may need no further action (other than documentation). The collection of additional information (e.g., monitoring, toxicological, or epidemiological data) might be needed to either validate the judgment of 'acceptability', or ensure that the risk mitigation measure(s) is performing as expected.

The outcome of a HHRA is an evaluation of potential health impacts that includes a qualitative or quantitative[10] analyses (or judgment) of the certainty of the effects (health impacts) and significance. Risk assessments are "conducted on a case-by-case approach giving full consideration to all relevant scientific information" (US EPA, 1986).

The justification for the selection or exclusion of particular methodologies and data sources should be considered and evaluated in terms of its limitations (of methods and data), and its implication to potential data gaps that may impact the adequacy or completeness of the HHRA (Bhatia et al, 2009; and US EPA, 1986).[11]

If the assessment determines that the health risk is (potentially) present, then specific recommendations to address the identified (or potential) health impacts, including

- decision alternatives,
- modifications to proposed policy, program, product, technology, process, project, etc., and mitigation measures or adaptive risk management strategies[12,13] are warranted (Bhatia et al, 2009).

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9 To better characterize the exposure profile, information may be generated through exposure monitoring, modeling, or biological monitoring (Mulhausen and Damiano, 2006).

10 In quantitative HHRA analyses, an estimate of the potential 'adverse health effects' risk on an individual, community, or population is derived by comparing the exposure concentrations with the relevant exposure limits (or protection goals), and the significance of the effect is then assessed.

11 e.g., uncertainty in predictions (due to assumptions or inferences made in the study), validity of evidence or findings, etc.

12 Environmental monitoring may be incorporated as part of the risk management plan to verify the effectiveness of the mitigation measures. Further long-term monitoring (or ongoing reassessment) may include ambient air monitoring, personal exposure monitoring, or periodic sampling of discharge streams or environmental media (e.g., water, soil, vegetation, fish, food, etc.) (Hopkins and Williams, 2011; Bhatia et al, 2009).

13 The review or discussion of risk management strategies is outside the scope of this document. Expert guidance should be sought regarding potential decisions or design alternatives and mitigations to ensure that they reflect current available and effective practices.

5. HHRA Guidance

General Health Canada (**HC**) and US Environmental Protection Agency (**US EPA**) risk assessment guidance documents are available for use in deterministic risk assessments (BC MOE, 2007); they are as follows:

- Guidance Documents related to Human Health Risk Assessment (**HC**) (http://www.hc-sc.gc.ca/ewh-semt/contamsite/docs/index-eng.php)
- Human Health Guidelines (**US EPA**) (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=54932#Download)
  - Guidelines for Exposure Assessment (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=15263#Download)
  - Exposure Factors Handbook (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12464#Download)
  - Child-Specific Exposure Factors Handbook (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=56747)
  - Supplemental Guidance for Assessing Susceptibility from Early Life Exposure to Carcinogens (www.**epa**.gov/ttn/atw/childrens_**supplement**_final.pdf)
  - Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (www.epa.gov/raf/publications/pdfs/AGEGROUPS.PDF)
  - Framework for Cumulative Risk Assessment (http://www.epa.gov/osa/spc/2cumrisk.htm) (www.**epa**.gov/raf/publications/pdfs/frmwrk_cum_**risk**_assmnt.pdf)
  - Guidelines for Health Risk Assessment of Chemical Mixtures (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=22567#Download)
  - Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=20533)
  - Guidelines for Cancer Risk Assessment (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=54932#Download)
  - Guidelines for Mutagenicity Risk Assessment (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=23160#Download)
  - Guidelines for the Health Assessment of Suspect Developmental Toxicants (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=23162#Download)
  - Guidance for PCBs: Cancer Dose-Response Assessment and Application to Environmental Mixtures (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12486)
  - Guidance for Quantitative Risk Assessment of Polycyclic Aromatic Hydrocarbons (PAHs) (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=49732)
  - Dermal Exposure Assessment: Principles and Applications (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=12188)
  - Framework for Metals Risk Assessment (www.epa.gov/raf/metalsframework/pdfs/metals-risk-assessment-final.pdf)
  - Microbial Risk Assessment Guideline: Pathogenic Microorganisms with Focus on Food and Water (http://www.epa.gov/raf/microbial.htm)[14]

It should be noted that the Health Canada's PQRA document focused on chemical contaminants *other than* petroleum hydrocarbon compounds (PHCs) and radiological contaminants. For PHCs[15], the Canadian Council of Ministers of the Environment has provided guidance documents[16], including spreadsheets to assist in the derivation of modified generic (Tier 2) soil quality guidelines that

[14] This document provides a framework for microbial risk assessment to determine health risks from food and waterborne pathogens (Nicol, 2013).

[15] PHCs are considered to be comprised of four fractions, and exclude known carcinogens such as benzene and benzo(a)pyrene (which are addressed as target compounds) (CCME, 2008).

[16] http://www.ccme.ca/ourwork/soil.html?category_id=43

incorporated limited site-specific data (BC MOE, 2007). For radiological contaminants, the Health Canada Guidelines for the Management of Naturally Occurring Radioactive Materials may be used[17]. BC MOE (2007) recommended that specific use of critical human receptors, physiological parameters, exposure routes and scenario assumptions, and associated equations abstracted from the relevant guidance document (e.g., for contaminated site risk assessments, use Tables 2, 3, 4, 5 and 6 Health Canada's *Federal Contaminated Site Risk Assessment in Canada Part I: Guidance on Human Health Preliminary Quantitative Risk Assessment (PQRA)*).

Note: For clarity, Health Canada's HHRA reference documents should be used (in preference over the US EPA's).

6. Reporting

Risk assessment results require a qualitative accompaniment; the HHRA report should describe or detail the following information to describe the significance, rationale, and strengths and weakness of that assessment:

- specific health concern analyzed,
- available scientific evidence and weight of that evidence,
- assumptions and defaults used,
- data sources and analytic methods used,
- existing (and, if available, baseline) condition(s),
- analytical results (and significance),
- limitations of exposure data, and
- health impact (characterization/assessment).
- Finally, the HHRA report should provide a prioritized list of recommendations (mitigation strategy, decision alternatives, adaptive risk management) to control or mitigate identified (or potential) health impacts.

[17] Exception: For the control of radioactively contaminated foods and public drinking water following a nuclear emergency in Canada, the reader should refer to the *Canadian Guidelines for the Restriction of Radioactively Contaminated Food and Water Following a Nuclear Emergency* (http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/emergency-urgence/index-eng.php).

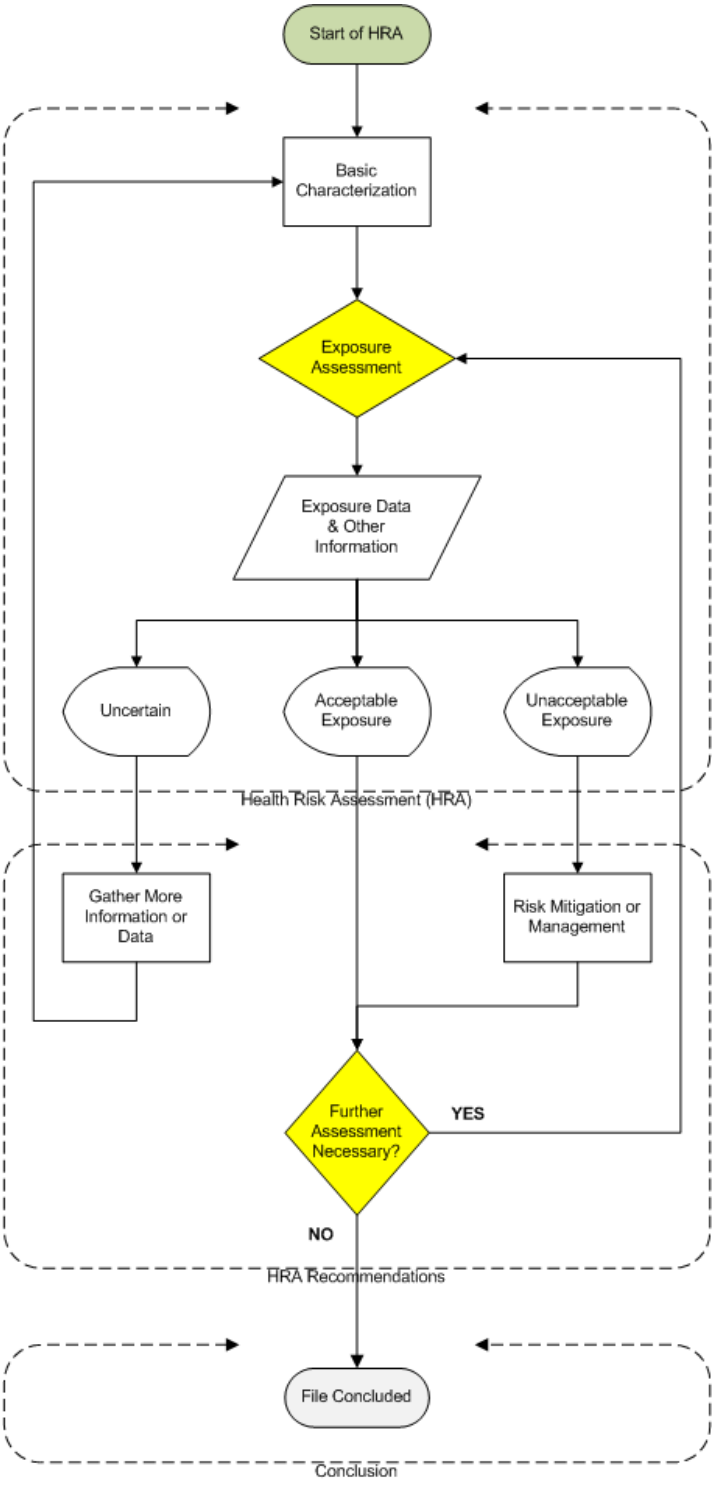

Figure 2. Strategy for assessing and managing environmental exposures[18]

[18] Adapted from Figure 1.2 in Mulhaussen and Damiano (2006).

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