Plain Language Explanation of Human Health Risk Assessment

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Oil Sands Research and Information Network

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REPORT SUMMARY

Many factors can affect a person's health, such as quality of life, how long they live, and whether or not they suffer diseases. These factors are referred to as *determinants of health*. The quality of environmental media related to oil sands developments in northeastern Alberta represents a concern to people at the local, national, and international level. The key determinants of people's exposure to chemical pollutants are: time-activity (where we spend time and what we do), interaction with indoor environments, diet, and occupation. In most instances these determinants explain most or all of what influences exposure to chemicals in the environment. One way to investigate the relationship between the quality of environmental media and human health risk is to perform a human health risk assessment (HHRA).

A human health risk assessment is an important component of most environmental impact assessments of new oil sands development projects. Human health risk assessment is also likely to be a key requirement for understanding potential human health impacts of the release of oil sands process-affected waters to the environment.

A human health risk assessment is the process of determining if a particular chemical or other hazard in the environment (e.g., particulate matter) poses a health risk to people for a specific set of conditions. People are called *receptors* in human health risk assessment. It is not possible to tell where in time and space people will actually be in relation to where chemical pollution exists, and therefore the extent to which they are actually exposed. Thus assumptions need to be made about their exposures to allow us to assess human health risk.

Human health risk assessments are prepared by professional consultants (scientists and engineers) for government, industry and other organizations. This is done to help decision makers, especially policy makers and regulators, understand potential health impacts from the release of chemical pollutants into the environment by industrial operations. This type of information – along with social, economic, and other information – can help to inform policy and regulatory decisions that help protect people from chemical exposures as a result of pollution.

Human health risk assessment procedures described here are normally accepted by regulatory agencies because they are, purposely, conservative. This conservatism makes it less likely to under estimate potential exposures and human risk and more likely that resulting regulatory decisions made will protect people from chemical pollution by industrial operations in real situations.

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1 INTRODUCTION

Many factors can affect a person's health, such as quality of life, how long they live, and whether or not they suffer diseases. These factors are referred to as *determinants of health* (Public Health Agency of Canada 2010). The physical environment only represents one of these determinants. As a determinant of health, the physical environment relates to people's interaction with environmental media (air water, soil, etc.).

The quality of environmental media related to oil sands developments in northeastern Alberta represents a concern to people at the local, national, and international level. One way to investigate the relationship between the quality of environmental media and human health risk is to perform a human health risk assessment (HHRA).

A human health risk assessment is an important component of most environmental impact assessments of new oil sands development projects (Alberta Environment 2011a,b). Appendix 1 provides more information on the use of human health risk assessment in environmental impact assessments in Alberta. Human health risk assessment is also likely to be a key requirement for understanding potential human health impacts of the release of oil sands process-affected waters to the environment.

There are two points to make before describing the human health risk assessment process. First, it is important to refer to human health risk (or human health impact) as *potential*. Despite our knowledge of and advances in science, all of the health assessment tools available to us today are – at best – limited in the ability to characterize human health risk when exposures to pollutants in the environment are small (National Research Council 1994). The term *potential* is used to indicate there may be a possibility of harm to humans (i.e., human health risk) from these exposures, but there is no certainty implied.

The other point to make is what science evidence tells us about actual exposures to chemical pollutants in the environment. Chemical pollutants from sources that are small and close to people are the most important for actual human exposure (Ott et al. 2007). In fact, the key determinants of people's exposure to chemical pollutants are (Baker et al. 2001, National Academy of Sciences 1991, Ott et al. 2007, U.S. EPA/AWMA 1989): time-activity (where we spend time and what we do), interaction with indoor environments, diet, and occupation. In most instances these determinants explain most or all of what influences exposure to chemicals in the environment.

1.1 Objectives of Report

This report will explain what a human health risk assessment is and how it is used to investigate the relationship between activities such as oil sands developments and human health risk. It will focus on oil sands developments; however the principles and procedures described here apply to any type of industrial development. Wherever possible, the report avoids scientific or technical jargon and uses plain language to explain the complex science and assumptions used in human health risk assessment. A general overview of the human health risk assessment process is presented to help understand how it is done.

1.2 What is a Human Health Risk Assessment?

A human health risk assessment is the process of determining if a particular chemical or other hazard in the environment (e.g., particulate matter) poses a health risk to people for a specific set of conditions (U.S. EPA 2010a). People are called *receptors* in human health risk assessment. It is not possible to tell where in time and space people will actually be in relation to where chemical pollution exists, and therefore the extent to which they are actually exposed. Thus assumptions need to be made about their exposures to allow us to assess human health risk.

A human health risk assessment is intended to help us understand the types of health impacts that may result if we assume that people are exposed to chemicals in the environment for a specific set of conditions. This involves addressing the following components (U.S. EPA 2010a):

- Identifying hazards in the environment (called environmental stressors) – such as chemicals or physical stressors like dust and heat – that people could be exposed to.
- Identifying the types of potential health problems that may be caused if we assume human exposure to these environmental stressors.
- Identifying people that are potentially exposed to these environmental stressors.
- Taking into account other influencing factors – such as genetics, pre-existing health conditions, sex, and age – to reflect the fact that some people are more susceptible to diseases than others.
- Estimating whether health impacts occur (the potential for harm) to these people from exposure.
- Describing uncertainties in the human health risk assessment to provide a proper perspective about limitations in the methods.

1.3 Who Prepares Human Health Risk Assessments and Why?

As early as the 1970s, safety engineers and radiation biologists were practicing something similar to risk assessment. Later, governments began to use methods referred to as risk assessment (Interagency Regulatory Liaison Group 1979). Today there is widespread public belief that the environment – particularly air, water and food quality – is being affected by the release of chemical pollutants from industrial operations.

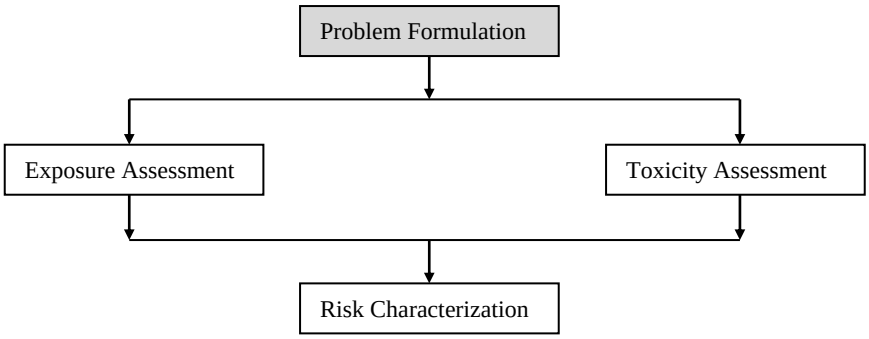
Human health risk assessments are prepared by professional consultants (scientists and engineers) for government, industry and other organizations. This is done to help decision makers, especially policy makers and regulators, understand potential health impacts from the release of chemical pollutants into the environment by industrial operations. This type of information – along with social, economic, and other information – can help to inform policy and regulatory decisions that help protect people from chemical exposures as a result of pollution (Agency for Toxic Substances and Disease Registry 2009, National Research Council 1994, Paustenbach 1989).

2 PREPARATION OF A HUMAN HEALTH RISK ASSESSMENT

There are four steps involved in preparing a human health risk assessment (Health Canada 2004, U.S. EPA 2010b):

- problem formulation
- exposure assessment
- toxicity assessment
- risk characterization

2.1 Problem Formulation



Problem formulation involves building an understanding of what chemicals are being released into the environment, how they are released from an activity (e.g., oil sands development project), and how people may be exposed to them (Health Canada 2004). The result of this step gives us an understanding of:

- what the contaminants of concern for potential human health impact are – *chemicals*
- how and where they are released into the environment, and what pathways they are in (e.g., air, water, food, or soil) – *exposure pathways*
- who may be exposed to them – *people*

These three components are initially evaluated for each contaminant of potential concern (referred to as *screening*) so that remaining steps of risk assessment only have to deal with chemicals, exposure pathways, and receptors that have a potential to cause harm.

2.1.1 *Contaminants of Potential Concern*

Contaminants of potential concern are chemicals or other hazards (e.g., particulate matter) released into the environment from an industrial project. They can be identified based on previous human health risk assessments and environmental impact assessment reports, or research. They can also be identified by considering individual process equipment that will be used in a project and what an equipment manufacturer says about the types of chemicals that will be emitted and how much will be emitted (emission factor data) from this equipment.

2.1.2 *Environmental Exposure Pathways*

An exposure pathway describes how a contaminant of potential concern travels through the environment from where it is released to people. An environmental exposure pathway consists of five elements (Agency for Toxic Substances and Disease Registry 2005):

- source of contamination
- environmental media (e.g., air, water, food, soil)
- point of exposure
- people
- route of exposure

Once released from a source, a contaminant of potential concern will travel through environmental media to points where exposure can occur. For humans, the major environmental media include air, water, food and soil. The point of exposure is the location where human contact with a contaminant of potential concern can occur.

For example, people can be exposed to contaminants of potential concern in the home, at work, or while vacationing at a lake, river or other body of water. Exposure can happen by breathing contaminated air, swimming in contaminated water, or consuming contaminated locally-caught fish.

An exposure route is how a contaminant can enter the human body. There are three general routes by which people can take contaminants into their bodies:

- inhalation (breathing in a contaminant as a gas or as particles in air)
- ingestion (swallowing something containing a contaminant; this can include food, water, and small amounts of soil)
- skin contact (being in contact with surface water or soil; some contaminants in water or soil can be absorbed through the skin)

Good ways to identify potential environmental exposure pathways include: understanding the physical, chemical, and biological properties of contaminants; understanding properties of environmental media; and, talking to people living and working in communities close to where contaminants are released into the environment.

Given a list of contaminants of potential concern, and knowing how exposure to each contaminant can occur, it is then possible to develop a complete list of all potential exposure pathways.

A figure can be used to illustrate the basic elements of exposure pathways (U.S. EPA 2010b) or the ways in which people might come into contact with environmental pollutants (Agency for Toxic Substances and Disease Registry 2005). An example of an exposure pathway for groundwater contamination is shown in Figure 1.

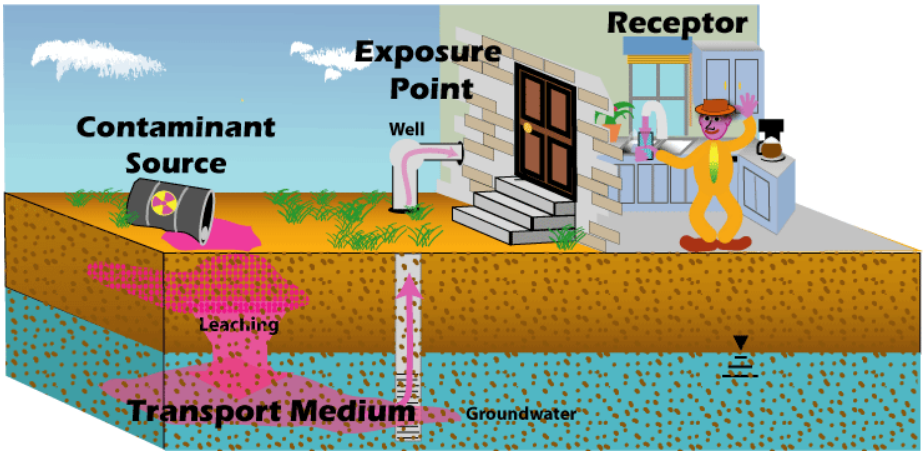


Figure 1. Conceptual exposure model for groundwater contamination (after Risk Assessment Information System 2009).

2.1.3 *Potential Receptors*

Receptors are people who may live near, visit, or perform an activity (e.g., work, recreation) that is close to existing or proposed oil sands developments. As a result, they may be exposed to contaminants of potential concern released from oil sands developments.

We often define receptors according to different stages of life. A human health risk assessment performed in Canada looks at five age groups (after Health Canada 2004):

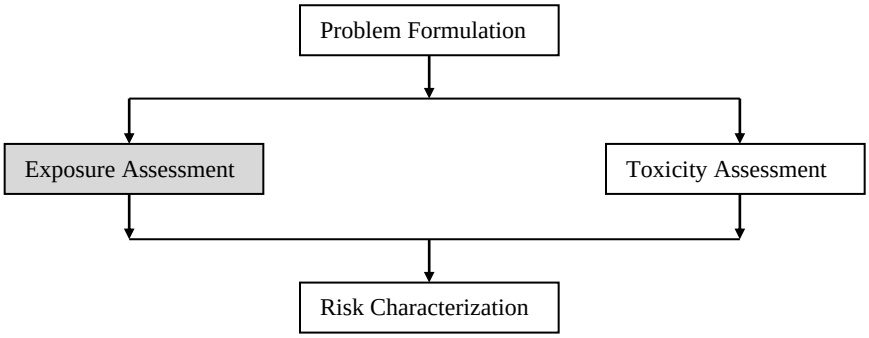
- infants (0 to 6 months old)
- toddlers (7 months to 4 years old)
- children (5 to 11 years old)
- teenagers (12 to 19 years old)
- adults (20 to 80 years old)

We are interested in these different life stages because we know that at different ages a person's exposure may be different. It is also important to consider children or elderly people separately as they might be more susceptible to exposure to chemicals than normal healthy teenagers and adults. Evaluation of health risks to children from environmental exposures is important for several reasons:

- their body organs are still developing

- their lifestyle (eating soil, crawling on the floor)
- they can receive higher exposures than adults since their body sizes are much smaller than adults

2.2 Exposure Assessment



Once exposure pathways are determined in the Problem Formulation stage, data are obtained and used to estimate (or predict) people's exposure to chemicals – how much, how often, and how long (U.S. EPA 2010b). This is called the Exposure Assessment. A general mathematical equation and assumptions for exposure factors used in calculating exposure are shown in Appendix 2. Together, this information is used to estimate people's exposure for different pathways.

Exposure can also be estimated through monitoring. However, when monitoring data are not available, computer modeling is used to estimate exposure. Computer modeling uses mathematical equations to look at how chemicals move through the environment and eventually reach a person. Because we do not want to underestimate exposure, it is normal to make cautious assumptions when we use these models (Williams and Paustenbach 2002). This is done to make sure that – if anything – we over-estimate people's exposure to chemicals (that is, a conservative approach to exposure estimation).

A person can be exposed to chemicals in a number of different ways – breathing air, contacting or drinking water, contacting dust and soil, eating food (Table 1). Traditional and country foods eaten by aboriginals, hunters and fishers are additional ways in which these people can be exposed to chemicals in the environment.

The amount, frequency, and duration of exposure to chemicals in the environment – called the exposure rate – depend on a number of factors, including (refer to Appendix 2):

- Concentration of chemicals in various environmental media (air, water, food, or soil).
- Characteristics of the chemicals (for example, their physical and chemical properties).

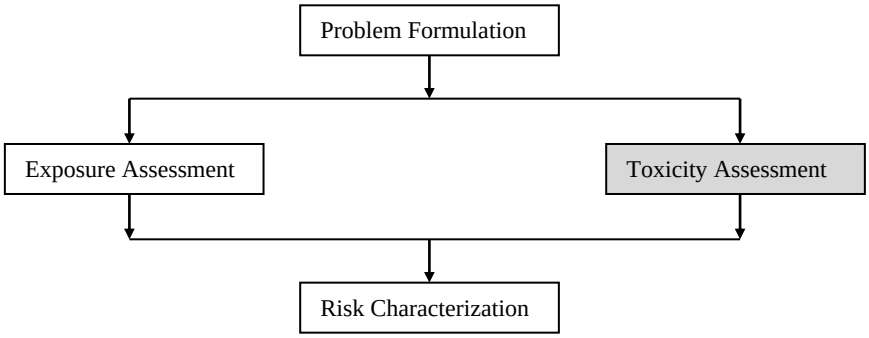
- Characteristics of the media that can affect how chemicals behave or move in the media.
- General physiological and behavioural characteristics of people (for example, breathing rates, activity patterns, contact rates with environmental media, etc.).

These characteristics are used to predict how much a person might be exposed to chemicals as they come into contact with the media through the exposure pathways.

Table 1. Examples of routes of exposure to chemical pollution grouped by environmental media (Agency for Toxic Substances and Disease Registry 2005, U.S. EPA 1989).

Environmental exposure media	Exposure point	Exposure route
Surface water	Agricultural, public, industrial and livestock water supplies	Ingestion, inhalation through volatilization, and skin contact
Groundwater	Wells and springs used for municipal, domestic, industrial and agricultural purposes	Ingestion, inhalation through volatilization, and skin contact
Soil	Recreational, agricultural, gardening and construction activities	Skin contact, ingestion, and inhalation
Air	Indoor or outdoor locations	Inhalation and skin contact
Sediment	Beach, river, sand bars, overbank flood deposits and other sandy areas along streams and in drainage ditches	Skin contact
Food	Fruits and vegetables in home gardens	Ingestion
Other	Contaminated or industrial sites	Ingestion, inhalation, and skin contact

2.3 Toxicity Assessment



Toxicity assessment is the process of judging whether exposure to a chemical can cause an adverse health effect (for example, cancer or birth defects) and whether the adverse health effect is likely to occur in humans. In the case of chemicals, this judgment is based on available

scientific evidence for a given chemical (or group of chemicals) and evidence linking the adverse health effect in humans to the chemical.

Scientific evidence used to classify human health hazards from low level exposures to chemicals in the environment comes from three types of information sources (enHealth 2002, Thomas and Hrudey 1997): animal studies, human studies, and vital statistics information. More details of these sources are provided in Appendix 3. The main outcome of this step is a determination of the *classification of potential* for a chemical to cause harm in people. It is referred to as a classification of potential for two very important reasons:

- There is no certainty implied in the potential for a chemical to cause harm if exposure to it is low enough. In fact, there is ample evidence to indicate that, for many chemicals, harm will not occur if human exposures are low enough (for example, Abelson 1994, Mattson and Calabrese 2010, Williams and Paustenbach 2002).
- The amount of exposure used to classify a chemical hazard from an animal experiment is virtually always much, much greater than the amount of environmental exposure that is of interest in human health risk assessment.

All chemicals are classified according to the following types of potential hazards:

Carcinogenicity – The ability or tendency of a chemical to cause cancer.

Mutagenicity – The ability or tendency of a chemical to cause genetic damage by damaging genes or chromosomes (including DNA damage).

Neurotoxicity – The ability or tendency of a chemical to adversely affect the structure or function of the central and/or peripheral nervous system.

Developmental/reproductive toxicity – The ability or tendency of a chemical to cause adverse effects on a developing fetus or on reproduction.

Other whole body effects – The ability or tendency of a chemical to cause some type of other specific whole-body adverse effect (for example, weight loss or other type of reversible effect).

For dose-response modeling purposes, the different potential hazard classifications described above are grouped into either of the following two health effects endpoints for all chemicals:

- noncancer (e.g., mutagenic, neurotoxic, developmental/reproductive toxic, and other whole-body effects)
- cancer

There is an established principle in toxicology… *the dose makes the poison*. Toxicity assessment also involves examining dose–response which is the relationship between exposure and the adverse health effect. Human exposure data for predicting adverse effects of chemicals are limited. Thus, laboratory animal studies have primarily served as the basis for most dose-response assessments.

Human exposures in the environment are always much, much smaller than doses tested in animal studies. Thus, methods for predicting biological responses at low doses based on what happens at high doses in animal studies, as well as predicting human responses based on the animal responses, are required and involve a major portion of dose response assessment.

2.3.1 *Noncancer Endpoints*

For all types of adverse effects endpoints other than cancer, the standard procedure used for evaluating dose-response aspects of chemical toxicity involves identifying the highest dose level among all the available experimental animal studies at which no adverse effect was observed (National Research Council 1994). This is referred to as a *no-observed-adverse-effect level* (NOAEL). Specifically, this is the highest exposure at which there is no statistically or biologically significant increase in the frequency of an adverse effect when compared with a control group.

A similar dose level is referred to as the *lowest-observed-adverse-effect level* (LOAEL). The lowest-observed-adverse-effect is the lowest exposure at which there is a significant increase in an observable effect from an experimental animal study. The lowest-observed-adverse-effect level is recognized to be more conservative than the no-observed-adverse-effect level (National Research Council 1986) because it is a higher value.

For example, if a chemical showed signs of liver damage in a laboratory rat study at a dose of 5 mg/kg per day, but no observable effect at 1 mg/kg per day and no other study indicated adverse effects at 1 mg/kg per day or less (National Research Council 1994):

- 5 mg/kg per day would be the lowest-observed-adverse-effect level
- 1 mg/kg per day would be the no-observed-adverse-effect level

Next, an uncertainty-factor approach is used to set a safe human exposure limit for the chemical. The idea is that if a no-observed-adverse-effect level can be identified from an animal study, it can be used as a threshold or level below which no adverse effects occur. The no-observed-adverse-effect level is adjusted downwards using uncertainty factors to set a safe exposure level for humans. If a person's exposure is below this safe exposure level, adverse effects are unlikely.

To establish a safe limit for human exposure, the experimental no-observed-adverse-effect level is divided by one or more uncertainty factors. Uncertainty factors are multiples of 10, which take into account uncertainty associated with predicting human responses based on animal responses, variation within the human population, and other factors. The mathematical equation that is used to establish a safe limit for human exposure to a chemical with a noncancer health effects endpoint is described in Appendix 4.

If a no-observed-adverse-effect level is derived from a high-quality animal study, fewer multiples of 10 are used. However, if the no-observed-adverse-effect level is derived from a less reliable animal study, or if only a lowest-observed-adverse-effect level was identified, more multiples of 10 are used to derive the safe exposure limit for humans.

The requirement for using uncertainty factors is not an exact science. It is based in part on the belief that humans could be more sensitive to the effects of a chemical than laboratory animals and the belief that variations in sensitivity exist within the human population (National Research Council 1994). These beliefs are reasonable, but the amounts of the differences between humans and animals for every chemical and adverse end point are often unknown. Using uncertainty factors in the manner described here is simply a way of accommodating these unknowns.

The safe exposure limit for a chemical is not an absolute dividing line between safety and danger such that exposures smaller than this limit are safe and exposures greater than this limit are not. It is important to note that exposures greater than a safe exposure limit only represent situations where the margin of safety for human health protection is judged to be smaller.

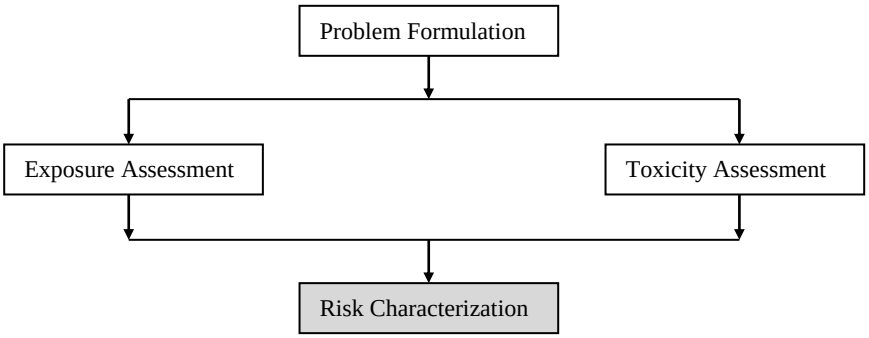
2.3.2 *Cancer Endpoints*

Dose-response assessment for cancer follows a different procedure from that for noncancer (National Research Council 1994, Williams and Paustenbach 2002). A science-policy assumption is made that no threshold for dose-response relationships exists or that, if one does exist, it is very low and cannot be reliably identified for chemicals that may contribute to cancer (National Research Council 1986).

The dose-response relationship for cancer in the low-dose region is assumed from theories that predict the response at the small doses anticipated for human exposure (Abelson 1994, enHealth 2002, National Research Council 1994). This procedure is based largely on an assumption that calls for caution in the face of scientific uncertainty. Additional technical details about the no threshold cancer dose-response assessment approach are provided in Appendix 4. It is important to note that other valid prediction models exist that give lower human cancer risks than the no threshold approach (Holland and Sielken 1993, Williams and Paustenbach 2002).

The dose of a chemical obtained from a human occupational epidemiology study or experimental animal study is extended to a lower dose which humans may be exposed to in the environment to predict an excess lifetime risk of cancer. An excess lifetime risk of cancer is the added risk of cancer resulting from a lifetime of environmental exposure to that chemical at a particular dose. It is referred to as *excess risk* because it represents the risk of cancer from lifetime exposure to a chemical in excess of the background risk of cancer that all individuals carry. For Albertans, the average background risk from all cancers is approximately 0.34 (or 34,000 in 100,000) over a lifetime based on 2010 statistics (this is shown in Appendix 5).

2.4 Risk Characterization



The final step of a human health risk assessment is referred to as risk characterization. Information developed and collected during the three previous steps is combined to produce quantitative and qualitative estimates of risks.

Quantitative estimates of risks for a chemical through an exposure pathway – called risk descriptions – are produced by dividing an estimated rate of exposure (determined in the exposure assessment) by a toxicity reference value (determined in the toxicity assessment). This result is an Exposure Ratio (ER). Appendix 6 provides more technical details of how Exposure Ratios are developed for noncancer and cancer health effects endpoints.

Exposure ratios are developed to quantitatively show the *potential for harm* to occur in receptors being investigated in risk assessment. Toxicity reference values can:

- be for noncancer or cancer endpoints
- apply to either a general population receptor or to an occupational receptor
- be based on short-term (acute) or long-term (chronic) exposure scenarios

The potential for harm from exposure to more than one chemical (chemical mixtures) is assumed to be additive by regulatory agencies based on policies designed not to possibly underestimate risk (Williams and Paustenbach 2002). This additive approach treats all chemicals as equal in their ability to cause harm, despite potential differences in the toxicological evidence used (for example, animal versus human data) in the toxicity assessment.

Additive interactions apply to chemicals that are mostly similar in their structure, impose biological interactions through similar mechanisms, and/or affect the same targeted organ.

Normally chemical exposures for ingestion and skin contact are combined. Combining chemical exposures for all pathways is more complex than for a single pathway because there are several points that need to be considered. There are two steps to determine whether two or more exposure pathways should be combined (Williams and Paustenbach 2002):

- identify reasonable exposure pathway combinations for chemicals
- examine whether it makes sense that the same receptors would consistently face the same type of chemical exposures by more than one pathway

The first step is straight-forward. To combine certain pathways, the same person or group of people need to be exposed to these pathways. If the pathways do not affect the same person or group of people, these pathways should not be combined. Furthermore, each pathway should be affecting the person or group of people in the same area and during the same time period because exposures might not occur in other locations or time periods (Williams and Paustenbach 2002).

During the second step, although some pathways may be combined, the same person or group of people may or may not experience the same type of exposures over the same period of time. In many cases it may be challenging to determine whether two or more exposure pathways should be combined. Where this is done, it is important to explain why pathways were combined, or why more than one pathway was used.

Risk characterization procedures mostly intentionally over-estimate the potential for harm, or attempt to generate overly conservative estimates of the potential for harm. The purpose of such evaluations is simply to rapidly identify those potential exposure scenarios worth further attention versus those that are clearly not important.

If estimated human health risks for a chemical through an exposure pathway are small from the analysis, a more refined evaluation is not needed – even though there may be significant data gaps or uncertainties in the procedures. However, if estimated risks are larger than a level recommended by regulatory agencies based on overly conservative assumptions, typically further qualitative analysis should be undertaken. This qualitative analysis is mostly done to develop a better understanding of what these conservative assumptions are and how they contribute to over-estimation. The reader is referred to Appendix 6 for more in-depth technical details about acceptable health risk levels recommended by regulatory agencies.

2.5 Uncertainty in Human Health Risk Assessment

Uncertainty is a measure of the "goodness" of an estimate. Without such a measure, it is impossible to judge how closely an estimated value relates to or represents reality. Uncertainty arises during all steps of human health risk assessment. Uncertainty in the exposure assessment, toxicity assessment, and risk characterizations steps are discussed here.

2.5.1 *Uncertainty in Exposure Assessment*

Exposure estimation always involves using a variety of information sources and analysis or modeling techniques. As a result, uncertainty is natural in the exposure assessment process (International Programme on Chemical Safety 2008). Two examples of sources of uncertainty that are important in the process are (U.S. EPA 1989):

- Assumptions and values used for parameters in the computer models to predict the amount of a chemical in environmental media.
- Assumptions of values for each of the parameters in the exposure assessment equation.

This uncertainty is partly handled in the process by making cautious assumptions for parameters in the computer models and during exposure estimation. This is done so that estimated exposures are more likely to be greater than the true exposure. For example, we estimate a person will drink more water than they actually do or that a chemical in water is present at a greater concentration that what it actually will be.

It is important to make sure that an explanation is provided about why these assumptions are made. A downside to always making cautious assumptions for these parameters and then combining them is that the resulting exposure can be much, much greater than the true value.

Always taking this approach increases our chances of falsely reaching a judgment that an exposure is high when it is not; or we might falsely take action to reduce an exposure when we do not have to. That is why people doing exposure assessments often revisit their assumptions to make sure – to the best of their ability – that the assumptions are reasonable.

2.5.2 *Uncertainty in Toxicity Assessment*

There are numerous sources of uncertainty in the toxicity assessment process that have been identified by others. Some of these are summarized in Table 4. A key uncertainty is whether a specific chemical is capable of causing the same adverse health effects in humans that were observed in animal studies (Williams and Paustenbach 2002). This relationship can be obvious for certain types of exposure situations.

For example, most chemicals that cause acute toxicity in the liver of a rat or mouse also show the same effect in humans for high dose (acute exposure) situations. However the same cannot be said of toxicity associated with low doses (exposures). Differences associated with absorption, distribution, metabolism, and excretion of a chemical between rats or mice (under high doses) and humans (under low doses) can be large.

Table 2. Examples of recognized general sources of uncertainty in the toxicity assessment process (enHealth 2002, National Research Council 1994, Williams and Paustenbach 2002).

Hazard Identification	Dose-response Assessment
Unidentified hazards Insufficient definition of incidence of an adverse outcome in a given study (positive negative association of incidence with exposure) Differences in study results for the same chemical Different study qualities for the same chemical: - how they are conducted - definition of control population - physical-chemical similarity of chemical studied to that of concern Different study types: - prospective, case-control, bioassay, *in vivo* (live animal), *in vitro* (cell culture) assays - test species, strain, sex, system - exposure route, duration Using the available hazard evidence from animal studies to represent health hazards in human populations	Definition of "positive responses" in a given study: - continuous versus semi-continuous exposure response data Procedures for parameter estimation Different dose-response sets between studies: - results - qualities - types Model selection for low dose risk prediction: - invalid low dose functional behaviour of dose-response relationship (threshold, sublinear, linear, supralinear, flexible) - role of time (dose frequency, rate, duration; age at exposure; fraction of lifetime exposed) Using results of tested doses in animal studies to represent human dose-response: - differences between absorption, distribution, metabolism, and excretion of large doses and small doses

The largest single source of uncertainty lies in the science-policy assumption used in the procedure to predict low dose-response in humans from high dose-response observations from animal studies (called the *linear extrapolation* procedure). The assumption is that what happens from giving large doses of chemicals to animals is also going to happen with small doses to humans (Abelson 1994). The assumption implies that pathways of metabolism of large doses and small doses are identical when in fact, this is not the case. Large doses of chemicals are accompanied by toxicity, cell death, and cell replacement. This creates conditions favorable for the growth of cancerous tumors. At small doses of the same chemical – in which cellular death does not occur – cancerous tumors would not be produced (Abelson 1994).

The U.S. EPA (1986) acknowledged this fact and states… *the linearized multistage procedure leads to a plausible upper limit to human risk that is consistent with some proposed mechanisms of carcinogenesis*. They go on to state that… *such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero. The range of risks, defined by the upper limit given by the chosen model and the lower limit which may be as low as zero, should be stated*.

Another key uncertainty is that it is difficult to predict the relationship between the dose needed to increase the cancer incidence in animals and that needed in humans (Williams and Paustenbach 2002). Sometimes it is even difficult to predict whether a chemical will be a human

carcinogen at any reasonable dose, even though it has been shown to cause cancer in animals. There are many reasons why a chemical may cause certain kinds of adverse effects in animals but not in humans. Difference in doses, absorption, metabolism, mechanisms of action, target tissue susceptibility, ability to repair DNA, and other factors can account for observed differences in the severity or type of adverse effects between animals and humans (Williams and Paustenbach 2002).

A number of uncertainties are related to the process of evaluating the dose-response relationship of a chemical. These include uncertainty in the selection of a particular animal study dataset; differences between absorption, distribution, metabolism, and excretion of large animal doses for a chemical versus small human doses, and model selection for low-dose prediction. The high- to low-dose prediction models tend to provide similar estimates of doses in the observable range, but can predict significantly different carcinogenic responses at the much-lower unobservable range.

2.5.3 *Uncertainty in Risk Characterization*

It is important for the reader to understand that risk assessments conducted in the manner described here are not estimates of the potential for chemicals to cause harm in real people. The procedures described here – while accepted for use by many regulatory agencies – only provide conditional estimates of the potential for chemicals to cause harm in people by making numerous assumptions about exposure and potential toxicity (U.S. EPA 1989). Therefore, it is important that the assumptions used and the uncertainties associated with them are clearly stated.

Uncertainties associated with risk characterization are the result of combined uncertainties in the exposure assessment and the toxicity assessment. These sources of uncertainties have been explained previously. One source of uncertainty that is unique to risk characterization, however, is the assumption that the total potential for harm associated with exposure to multiple chemicals through multiple pathways is equal to the sum of the individual chemical risks and pathways.

3 INTERPRETATION OF RISK ASSESSMENT RESULTS

A general outline of a human health risk assessment report for an industrial project in Alberta is provided in Table 3. This outline is discussed further to provide the reader with details of what would be expected to be in a human health risk assessment report.

1. An introduction should contain specific information about the objectives of the risk assessment. A section should also be included discussing risk assessment methods used and providing scientific references upon which the methods are based (for example, Health Canada, U.S. Environmental Protection Agency, World Health Organization).

Table 3. General outline of a human health risk assessment report for an industrial project in Alberta.

1 Introduction
- Overview
- Objectives of risk assessment
- Organization of report

2 Human health risk assessment procedures

3 Problem Formulation
- Descriptions of exposure scenario cases (baseline case, application case, and planned development case)
- Description of spatial boundaries
- Description of temporal boundaries
- Identification of contaminants of potential concern
  - Special contaminants of potential concern (e.g., exposure to fine particulate matter, dust, microorganisms)
- Identification of exposure pathways
  - Conceptual human exposure model
- Identification of potential receptors
  - Intake rate relationships for exposure pathways
  - Exposure parameters for potential receptors
- Description of Uncertainties

4 Toxicity Assessment
- Classification of hazards for contaminants of potential concern
  - Noncancer endpoints
  - Cancer
  - Special contaminants of potential concern
- Toxicity reference values for contaminants of potential concern
  - Noncancer endpoints
  - Cancer
  - Special contaminants of potential concern
- Description of uncertainties

5 Risk Characterization Results
- Baseline case
  - Noncancer endpoints
  - Cancer
  - Special contaminants of potential concern
- Application case
  - Noncancer endpoints
  - Cancer
  - Special contaminants of potential concern
- Planned development case
  - Noncancer endpoints
  - Cancer
  - Special contaminants of potential concern
- Description of uncertainties

6 Conclusions

7 References

8 Appendix

2. A section should be devoted to problem formulation. Exposure scenarios normally investigated for an environmental impact assessment should be explained.

   The regional (spatial) boundaries and the timescale in which the risk assessment applies should be described here. It is reasonable to expect that limits would apply to the regional scale at which potential health impacts are examined in the risk assessment. A cautious timescale to consider for the risk assessment is lifetime.

   Contaminants of potential concern should be identified along with rationale for including them in the risk assessment. In some cases, there may be separate discussion devoted to special contaminants of potential concern, such as fine particulate matter or other contaminants of potential concern that have unique exposure circumstances and/or health effects endpoints.

   Environmental exposure pathways and people included in the health risk assessment should be identified and discussed here; those that are not included in the risk assessment should be described, and reasons given why they are not included.

   Intake rate relationships for exposure pathways should be clearly shown so that readers understand how exposure rates are being estimated for individual pathways. In addition, values for exposure parameters should be provided for different potential receptors evaluated in the risk assessment. Often, this information is placed in an appendix because of its technical detail.

   It is not necessary to expect to see estimated intake rate results in the risk assessment as these results are normally shown later in the document. Finally, readers should expect to see some discussion of where uncertainty is apparent in exposure assessment and the types of cautious assumptions that were made to over-estimate exposure to potential receptors.

3. The Exposure Assessment should be included (with all the modeling results, the assumptions made in the model, all calculations, all measured data used, predicted daily intakes, and a worked example to show the reader how the risk assessor got their results – complete transparency so everything can be replicated).

4. The toxicity assessment should contain two key types of information for the contaminants of potential concern. The first is the hazard classification information associated with each contaminant of potential concern. Specifically, these are health effects endpoints (noncancer or cancer) descriptions; and they should be accompanied with scientific references. In some cases this information may be placed in an appendix because of its technical detail. The second type of information that should be shown is toxicity reference values for each contaminant of potential concern for these health effects endpoints. Scientific references supporting these toxicity reference values should be provided.

   The toxicity assessment should also contain a discussion that provides the reader with a sense of the uncertainty in toxicity assessment of chemicals.

5. Results are provided and discussed in the risk characterization step. Often there will be many pages of Exposure Ratios (ERs) tabulated for key potential receptors (that is, the ones that receive the highest exposures), and for each exposure pathway and exposure scenario. Because it is possible that many pages of tabulated exposure ratio results will be presented it is very important to expect that key results are highlighted and discussed further in this section.

   For example, only those results with high exposure ratios would be discussed further. Specifically, key results of the risk characterization step that should be discussed include individual contaminants of potential concern (or combinations of contaminants of potential concern – chemical mixtures) and environmental exposure pathways (or combinations of environmental exposure pathways) that have higher exposure ratios.

   Finally, a proper perspective of the roles of uncertainty and conservatism in the overall risk assessment process should be discussed. These discussions of uncertainty and conservatism related to risk characterization results should not imply that human health risk is greater than the results. It is normally expected that – because of conservative assumptions – human health risk is less than what the results indicate. As stated previously by the U.S. EPA (1986): in the case of chemicals that may contribute to cancer, human health risk may be as low as zero.

6. A final component that should be discussed is conclusions of the process. A general sense of the magnitude of potential human health risk (impact) of a proposed project – such as negligible, low, moderate, etc. – should be stated for contaminant of potential concerns with higher exposure ratios. This section should also discuss the role of uncertainty for these contaminants of potential concern.

Government agencies rely on human health risk assessment results to understand potential health impacts from the release of chemical pollutants into the environment by industrial operations, including oil sands developments. These agencies use risk assessment results to make policy and other regulatory decisions as to whether or not these operations should proceed and if they do, what actions may be necessary to reduce health risks.

As stated previously, these decisions are not solely based on human health risk assessment results. Other types of information are also considered – such as social, economic, and other information – to help agencies make the best possible policy and regulatory decisions to protect people from chemical pollution by industrial operations. Members of the public, on the other hand, may look to the results of risk assessment to seek answers to questions such as:

- What health effects are caused by chemical pollution from an industrial operation?
- What do the risk characterization results mean?
- How much risk is acceptable?
- What happens when the limits for acceptable risk are exceeded?

Human health risk assessment procedures described here are normally accepted by regulatory agencies because they are, purposely, conservative. This conservatism makes it less likely to under estimate potential exposures and human risk and more likely that resulting regulatory decisions made will protect people from chemical pollution by industrial operations in real situations. On the other hand, there is no guarantee that these risk assessment procedures will provide results that answer specific questions the public may have about risk.

4 ACRONYMS

AT	Averaging time
ATSDR	Agency for Toxic Substances & Disease Registry
AWMA	Air & Waste Management Association
BW	Body weight
C	Chemical concentration
COPC	Contaminant(s) of Potential Concern
ED	Exposure duration
EF	Exposure frequency
EIA	Environmental Impact Assessment
ER	Exposure Ratio
I	Intake rate of chemical
ILCR	Incremental lifetime cancer risk
IR	Intake rate of the contaminated media
LOAEL	Lowest-observed-adverse-effect-level
NOAEL	No-observed-adverse-effect-level
OSRIN	Oil Sands Research and Information Network
$PM_{2.5}$	Fine particulate matter
RsC	Risk-specific concentration
RsD	Risk-specific dose
SEE	School of Energy and the Environment
SO_2	Sulphur dioxide
TRV	Toxicity reference value
UF	Uncertainty factor
U.S. EPA	United States Environmental Protection Agency

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APPENDIX 1: Human Health Risk Assessment in Environmental Impact Assessments

Human health risk assessments are a requirement for most environmental impact assessments (EIAs) of industrial operations (Brown and Lee 2009). Alberta Environment (2011a,b) provides information on how they are used in EIAs in Alberta.

To understand the types of exposure pathways in the environment for chemicals, it is first necessary to describe the situations (or scenarios) in which the exposure pathways will exist. For environmental impact assessments in Alberta, this is normally done by considering three different cases:

- A baseline case.
- An application case (the baseline case plus the proposed project).
- A planned development (or cumulative) case (the application case plus any known future developments).

These three exposure scenarios are additive in terms of emissions of chemical pollutants and potential exposures, and the corresponding potential human health risk that occurs under each scenario:

- The *baseline case* is used to show potential exposures and human health risk (potential for harm) using standard assumptions for chemical toxicity and receptor exposure factors, and with potential exposures arising from baseline emissions of chemical pollutants. The baseline case also serves to set the bar for what is currently "acceptable" by virtue of having been approved by regulators on behalf of the public.

  The baseline case exposure scenario represents emissions of chemical pollutants from existing industrial facilities, approved industrial facilities, and other emission-related activities (for example, motor vehicle emissions) in a study area. Approved industrial facilities are activities which have regulatory approval by a federal, provincial, or municipal authority but are not in operation yet.

  Emissions can be based on maximum equipment or process rates for industrial facilities. In cases where no emission rate information is available from approved projects, sometimes human health risk assessments will use the measured environmental quality data in the study area (e.g., for air) to represent the baseline conditions.

- The *application case* is used to show the incremental change in human health risk using the same standard assumptions for chemical toxicity and receptor exposure factors as the previous case; however, with potential exposures corresponding to baseline plus proposed project emissions of chemical pollutants.

- The *planned development (or cumulative) case* is used to show the incremental change in human health risk using the same standard assumptions for chemical toxicity and receptor exposure factors as the previous cases; however, with potential exposures corresponding to emissions of chemical pollutants from baseline plus

proposed project plus all other planned (future) industrial projects or activities that are proposed and on public record in a study area.

A proposed project's potential incremental impact to human health risk in a study area can be shown by comparing results of the application case to the baseline case. The potential cumulative impact to human health risk in a study area can be shown comparing results of the planned development (or cumulative) case to the baseline case.

It is important to note that new contaminants of potential concern may be added with each of the cases.

APPENDIX 2: Exposure Calculations in Human Health Risk Assessment

Intake Rate

The rate of exposure for a person is estimated using the following general equation (some call this an *intake rate* or *dose*) (U.S. EPA 1989, 2010a):

$$E = \frac{C \times IR \times EF \times ED}{BW \times AT}$$

where:

- E = Exposure rate, or the amount of chemical taken in by the exposure route (milligrams of chemical per kilogram body weight per day or mg/kg/day).
- C = Chemical concentration, or the average concentration of the chemical over the exposure period (for example, for a surface water exposure pathway it would be milligrams of chemical per litre of water – or mg/L).
- IR = Intake rate of the contaminated media (for example, for an air exposure pathway it would the cubic metres of air inhaled per day – or m^3/day).
- EF = Exposure frequency, or the number a times during a year that an exposure event occurs where a person is exposed to contaminated media (in days per year – day/yr).
- ED = Exposure duration, or the number of years over which the exposure event occurs (yr).
- BW = Body weight, or the weight of the person in kilograms (kg).
- AT = Averaging time, or the total over which the exposure event occurs (days).

This equation is for estimating exposures that occur daily, and other types of occur that do not occur daily – such as exposures related to seasonal activities (swimming in the summer in a contaminated lake) or exposures that occur at work (only five days a week). Health Canada (2004) provides values for some of the parameters for physical characteristics of various people (Tables 4 and 5). These include body weight (BW), soil ingestion rate, inhalation rate, water ingestion rate, skin surface area, and food ingestion rate (rates of consuming root vegetables, other vegetables, and fish for the Canadian general population and the Canadian aboriginal population).

Table 4. Recommended human receptors and their characteristics for preliminary quantitative risk assessments (after Health Canada 2004).

Receptor Characteristic	Infant	Toddler	Child	Teen	Adult	Construction Worker
Age	0 to 6 months	7 months to 4 years	5 to 11 years	12 to 19 years	20 years	>20 years
Body weight (kg)	8.2	16.5	32.9	59.7	70.7	70.7
Soil ingestion rate (g/d)	0.02	0.08	0.02	0.02	0.02	0.1
Inhalation rate (m^3/d)	2.1	9.3	14.5	15.8	15.8	15.8
Water ingestion rate (L/d)	0.3	0.6	0.8	1.0	1.5	1.5
Time spent outdoors (hr/d)	varies	varies	varies	1.5	1.5	8
Skin surface area (cm^2):						
Hands	320	430	590	800	890	890
Arms (upper and lower)	550	890	1480	2230	2500	2500
Legs (upper and lower)	910	1690	3070	4970	5720	5720
TOTAL	1780	3010	5140	8000	9110	9110
Soil loading to exposed skin (mg/cm^2/event):						
Hands	0.1	0.1	0.1	0.1	0.1	1
Surfaces other than hands	0.01	0.01	0.01	0.01	0.01	0.1
Food ingestion (g/day):						
Root vegetables	83	105	161	227	188	not applicable
Other vegetables	72	67	98	120	137	
Fish	0	56	90	104	111	

Table 5. Additional recommended human receptors and their characteristics for preliminary quantitative risk assessments of Canadian aboriginal populations (after Health Canada 2004).

Canadian Aboriginal Population						
Receptor Characteristic	**Infant**	**Toddler**	**Child**	**Teen**	**Adult**	**Construction Worker**
Age	0 to 6 month	7 month to 4 year	5 to 11 year	12 to 19 year	20 year	>20 year
Food ingestion (g/day):						
Fish	0	95	170	200	220	not applicable
Wild game	0	85	125	175	270	

APPENDIX 3: Evidence used to Classify Human Health Hazards

The scientific evidence used to classify human health hazards from low level exposures to chemicals in the environment (enHealth 2002, Thomas and Hrudey 1997) comes from animal studies, human studies, and vital statistics information:

1. Animal toxicology data. These data are from toxicological studies on live animals (*in vivo*); or from cellular assay (*in vitro*) tests to identify the potential for a chemical to cause harm at the cellular level.
2. Human epidemiology data. These data are from studies on human populations and are related to the study of diseases and their distribution in the population. Provincial and national health care databases that record population rates of specific diseases – such as various types of cancers – and other outcomes are also of interest.
3. Human vital statistics data. Vital statistics are data concerning important events in human life. Provincial and national databases that record deaths along with related causes are of interest.

The most convincing line of evidence for human health risk is a well-conducted epidemiology study in which a positive association between exposure and disease has been observed (National Research Council 1994). Human statistics from provincial or national health care databases and vital statistics departments can also offer direct and convincing evidence of the potential for harm if it can be understood what the underlying risk factors are for the diseases and/or deaths in the population. If these types of data are unavailable or insufficient, and they usually are, animal data are then used to classify the potential for chemicals to cause harm in humans (National Research Council 1994, Williams and Paustenbach 2002).

In this case, data obtained from laboratory animal studies – using rats, mice, rabbits, monkeys, dogs, etc. – are used to make inferences (assumptions) about the potential for chemicals to cause harm in humans. These animal experiments can be designed, controlled, and conducted to address specific gaps in knowledge about the potential for chemicals to cause harm in humans.

Animal experiments have the advantage of being performed under controlled laboratory conditions. However, uncertainties exist in hazard information obtained from animal experiments because the effects of the vast majority of chemicals have not been studied in human bodies. Effects in animals do not necessarily imply similar affects in humans (U.S. EPA 2010a, Williams and Paustenbach 2002). As a result, numerous assumptions are needed to be able to link hazard information from laboratory animal studies to humans for many chemicals (National Research Council 1983).

A wide variety of animal experiments and analysis are used to support hazard identification (U.S. EPA 2010a). The two basic types of information that are of interest include toxicokinetics and toxicodynamics.

Toxicokinetic Information

Toxicokinetics involves the study of the rate at which substances foreign to the body are absorbed, distributed, metabolized, and excreted or eliminated within a living system. This information is extremely valuable to toxicologists. For example, this type of information helps explain why consuming small amounts of alcohol (ethanol) over a short time period is not considered harmful. This is because the biological processes described above are able to eliminate ethanol from the blood stream. However, consuming large amounts alcohol over a short period can lead to a state referred to as alcohol poisoning because the biological processes cannot eliminate ethanol from the blood stream fast enough.

Toxicodynamic Information

Toxicodynamics involves the study of effects that chemicals have on the human body. Here one is interested in understanding the ways in which a chemical may affect human health and how much (the dose) of the chemical is required to cause these effects.

Another key component of hazard identification involves evaluating the weight of evidence regarding a chemical's potential to cause adverse health effects (or harm). A weight of evidence description would typically provide information about certain *threshold levels of evidence* and *confidence in the evidence* for a particular chemical, such as (U.S. EPA 2010a):

- evidence indicating that a chemical is carcinogenic to humans
- suggestive/some evidence of a chemical's carcinogenic potential
- evidence suggesting lack of carcinogenicity
- no evidence of a chemical's carcinogenic potential
- inadequate data to determine whether a chemical is carcinogenic to humans

APPENDIX 4: Dose-Response Assessment Approaches

Threshold Dose-Response Assessment Approach for a Chemical with Noncancer Health Effects

To establish a safe limit for human exposure, the experimental no-observed-adverse-effect level (NOAEL) is divided by one or more uncertainty factors. Uncertainty factors are multiples of 10, which take into account uncertainty associated with predicting human responses based on animal responses, variation within the population, and other factors. The equation used to estimate a safe exposure limit is:

$$\text{Safe exposure limit} = \frac{\text{animal study NOAEL or LOAEL}}{UF_1 \text{ x } UF_2 \text{ x } \ldots \text{ x } UF_i}$$

Uncertainty factors (UF_i's) used in the equation are:

- UF_H: A factor of 10 is used to represent human heterogeneity to account for variation of sensitivity within the human population.
- UF_A: A factor of 10 is used to represent variation in responses between experimental animals and humans.
- UF_S: A factor of 10 is used to represent possible variation in responses for subchronic versus chronic exposure conditions and to take into account possible variation between a NOAEL derived from less than lifetime (subchronic) animal study versus a lifetime (chronic) animal study.
- UF_L: A factor of 10 is used to represent use of a LOAEL instead of a NOAEL to account for having to rely upon the LOAEL if a NOAEL has not been measured.
- UF_D: A factor of 10 is used to represent adequacy of the animal study database to account for uncertainty in having to rely upon incomplete data.

In some cases a modifying factor (MF) up to a value of 10 is used to represent quality of data available. If a NOAEL is derived from a high-quality animal study, fewer multiples of 10 are used. However, if the NOAEL is derived from a less reliable animal study – or if only a lowest-observed-adverse-effect level (LOAEL) was identified, more multiples of 10 are used to derive the safe exposure limit for humans.

No Threshold Cancer Dose-Response Assessment Approach

The approach involves using a statistical/mathematical linear curve fitting procedure. An example of this is the linearized multistage model used by the U.S. Environmental Protection Agency (U.S. EPA 2010a). The result of this curve fitting procedure is called a *potency factor*.

The potency factor is obtained from a linear dose-response curve that is fit to experimental animal dose data at the high end, with the lower end of the curve passing through zero dose. A statistical upper-bound 95% confidence limit relationship is then determined from this fitted curve. The slope of the upper-bound 95% confidence limit relationship in the low-dose region is the potency factor.

The potency factor is taken to represent an upper-bound estimate of the lifetime probability of an individual developing cancer, as a result of a certain level of exposure to a chemical. The excess lifetime risk of cancer – or excess risk – is then represented as (U.S. EPA 2010a):

$$\text{Excess risk} = \text{Exposure (mg/kg per day)} \times \text{potency factor (mg/kg per day)}^{-1}$$

It is referred to as *excess risk* because it represents the risk of cancer from lifetime exposure to a chemical in excess of the background risk of cancer that all individuals carry.

The curve fitting procedure that is used to derive the potency factor involves considerable uncertainty because the shape of the dose-response curve in the low-dose region (Figure 2) is not derived from experimental observation. Rather, what happens in the low-dose region is assumed from theories that predict the shape of the curve at the low doses anticipated for human exposure (Abelson 1994, enHealth 2002, National Research Council 1994).

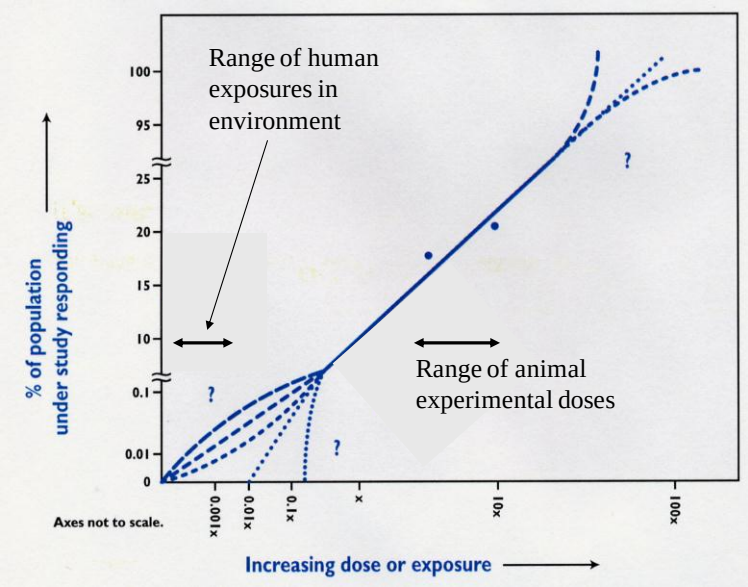

Figure 2. Prediction of dose-response in the low-dose range from high-dose experimental animal studies (after enHealth 2002).

This procedure is based largely on the science-policy assumption that calls for caution in the face of scientific uncertainty. Other valid prediction models exist that give lower human cancer risks (Holland and Sielken 1993, Williams and Paustenbach 2002). Although the actual human cancer risk cannot be known using this procedure, it is thought that it will not exceed the upper bound, it might be lower, and it could even be zero (National Research Council 1994, U.S. EPA 1986).

APPENDIX 5: Estimated Individual Lifetime Background Cancer Risk for Albertans

The individual lifetime background cancer risk for Albertans for all cancers combined can be estimated by combining life expectancy data for Alberta (after Statistics Canada 2010) with the annual risk of all cancers for Alberta from the most recent Canadian cancer statistics (Canadian Cancer Society 2011):

1. An assumption is first made that the annual risk of all cancers is the same for all individuals in Alberta and is constant for all individuals over a lifetime.
2. The Canadian Cancer Society (2011) reports that the estimated age-standardized incidence rate for all cancers in 2010 in Alberta is:
   - 467 in 100,000 for 1,737,000 males
   - 374 in 100,000 for 1,709,000 females
3. Using these data, the population weighted age-standardized incidence rate per 100,000 for all cancers in Alberta in 2010 can be estimated:

$$\frac{(467\ x\ 1{,}737{,}000) + (374\ x\ 1{,}709{,}000)}{(1{,}737{,}000 + 1{,}709{,}000)} = 421$$

   This value – 421 in 100,000 – can be used to represent the average annual background risk of all cancers for an individual in Alberta.
4. The life expectancy at birth in 2005/2007 is reported to be 80.5 years (average of both sexes) in Alberta (Statistics Canada 2010).
5. Therefore, the "lifetime" average background risk of all cancers for an individual in Alberta is:

421 in 100,000 per year *x* 80.5 years = 33,890 in 100,000 (or ~34,000 in 100,000).

APPENDIX 6: Technical Procedures for Risk Characterization

Risk Descriptions

Noncancer endpoints – For chemicals that may contribute to noncancer endpoints, toxicity reference values are *safe exposure limits* derived from the dose-response assessment. For example, the U.S. Environmental Protection Agency has a safe exposure limit for oral exposure to ethylbenzene (referred to as a Reference Dose) of 0.1 mg/kg per day (U.S. EPA 1991). This is a long-term (chronic) exposure limit that can be used in risk assessment to examine the potential for harm from oral (ingestion or skin contact) exposure to ethylbenzene for receptors.

Toxicity reference values can also represent safe exposure concentrations. For air pollutants such as sulphur dioxide (SO_2), fine particulate matter ($PM_{2.5}$), or other air pollutants, toxicity reference values can be based on established ambient air quality objectives or guidelines. For example, the Alberta ambient air quality 1-hour objective for ethylbenzene is 2,000 $\mu g/m^3$ (Alberta Environment 2010). This is a short-term air quality limit that can be used in a risk assessment to examine the potential for harm from an acute (short-term) inhalation exposure to ethylbenzene for receptors.

The comparison for noncancer endpoints is made by calculating an Exposure Ratio.

1. An Exposure Ratio (or ER) for an oral (ingestion or skin contact) exposure pathway is calculated by dividing a predicted exposure rate determined in the exposure assessment by the corresponding safe exposure limit for a specific chemical, as indicated in the following equation:

$$\text{Exposure Ratio (ER)} = \frac{\text{Exposure rate (mg chemical per kg body weight per day)}}{\text{Safe exposure limit (mg chemical per kg body weight per day)}}$$

2. An Exposure Ratio for an inhalation pathway is calculated by dividing a predicted inhalation exposure concentration determined in the exposure assessment by the corresponding air quality objective for a specific chemical, as indicated in the following equation:

$$\text{Exposure Ratio (ER)} = \frac{\text{Inhalation exposure concentration } (\mu g/m^3)}{\text{Air quality objective or guideline } (\mu g/m^3)}$$

The safe exposure limit for a chemical is not an absolute dividing line between safety and danger such that exposures smaller than this limit are safe and exposures greater than the limit are not. Exposures greater than the safe exposure limit, at most, represent situations where the margin of safety for human health protection is smaller. Thus, exposure ratios less than 1 indicate that exposures are unlikely to result in any harm, while exposure ratios greater than 1 indicate that the margin of safety for human health protection is smaller and there may be a concern for potential noncancer effects.

Cancer – For chemicals that may contribute to cancer, toxicity reference values are *risk-specific doses* or *risk-specific concentrations* derived from the dose-response assessment. This is explained further below. The comparison for cancer endpoints can be made in several ways:

1. In the first way, an incremental lifetime cancer risk (or ILCR) can be estimated for oral (ingestion and skin contact) exposure to a chemical that may contribute to cancer. This is the same as the excess risk that was described in Section 2.3.2:

ILCR (or excess risk) = Exposure rate (mg/kg per day) × potency factor $(\text{mg/kg per day})^{-1}$

The incremental lifetime cancer risk is then compared to an acceptable excess cancer risk level that is used by regulatory agencies for public health protection. In Alberta, it is normal to apply an acceptable excess cancer risk level of 1 in 100,000 (or 10^{-5}) to an individual receptor for use in human health risk assessment of chemicals associated with Environmental Impact Assessments (Health Canada 2004).

This level of acceptable excess cancer risk requires some explanation. It is intended to indicate that it is deemed acceptable if lifetime exposure to a chemical increases a person's chance of developing cancer by 1 in 100,000 or less. This level appears quite reasonable when it is compared to the average background risk of cancer (for all cancers) that Albertans carry – 34,000 in 100,000 over a lifetime. The acceptable excess cancer risk (1 in 100,000) is more than 30,000 times smaller than the average background risk of cancer (for all cancers) that individual Albertans carry.

Several provincial agencies across Canada (British Columbia, Alberta, and the Atlantic provinces) use an acceptable excess lifetime cancer risk of 1 in 100,000 in the regulatory programs (Health Canada 2004). Incremental lifetime cancer risks less than 1 in 100,000 indicate that exposures are unlikely to result in any harm, while incremental lifetime cancer risks greater than 1 in 100,000 indicate that there may be concern for potential cancer effects.

2. Alternatively, it is also possible to calculate a *risk-specific dose* (or RsD) for oral (ingestion and skin contact) exposure to a chemical that may contribute to cancer. A risk-specific dose for a chemical that may contribute to cancer is a dose corresponding to a specified risk level, in this case using 1 in 100,000 as the specified risk level.

An Exposure Ratio (or ER) for an oral (ingestion or skin contact) exposure pathway can then be calculated by dividing a predicted exposure rate determined in the exposure assessment by the corresponding risk-specific dose for the chemical that may contribute to cancer, as indicated in the following equation:

$$\text{Exposure Ratio (ER)} = \frac{\text{Exposure rate (mg chemical per kg body weight per day)}}{\text{RsD (mg chemical per kg body weight per day)}}$$

Exposure ratios less than 1 indicate that exposures are unlikely to result in any harm, while exposure ratios greater than 1 indicate that the margin of safety for human health protection is smaller and there may be concern for potential cancer effects.

3. Finally, a *risk-specific concentration* (or RsC) for inhalation exposure to a chemical that may contribute to cancer can be calculated. A risk-specific concentration for a chemical that may contribute to cancer is a concentration corresponding to a specified risk level, in this case using 1 in 100,000 as the specified risk level.

   An Exposure Ratio (or ER) for an inhalation exposure pathway can then be calculated by dividing a predicted inhalation exposure concentration determined in the exposure assessment by the corresponding risk-specific concentration for the chemical that may contribute to cancer, as indicated in the following equation:

$$\text{Exposure Ratio (ER)} = \frac{\text{Inhalation exposure concentration } (\mu g/m^3)}{\text{RsC } (\mu g/m^3)}$$

   Exposure ratios less than 1 indicate that exposures are unlikely to result in any harm, while exposure ratios greater than 1 indicate that the margin of safety for human health protection is smaller and there may be concern for potential cancer effects.

Additivity of Potential Health Effects

Noncancer endpoints – The potential for harm from simultaneous exposure to more than one chemical (chemical mixtures) that may contribute to noncancer effects is assumed to be additive by regulatory agencies based on policies designed not to possibly underestimate risk (Williams and Paustenbach 2002). Specifically, the potential for harm for these conditions can be evaluated by summing the Exposure Ratios (ERs) for individual chemicals:

$$\sum ER = ER_1 + ER_2 + \ldots + ER_i$$

Where ER_i = Exposure Ratio for the i^{th} chemical.

The additive approach treats all chemicals as equal in their ability to cause harm, despite potential differences in the underlying toxicological evidence used (for example, animal versus human data). Additive interactions apply to chemicals that are mostly similar in their structure, impose biological interactions through similar mechanisms, and/or affect the same targeted organ. Finally, short-term (acute) or long-term (chronic) exposure scenarios are evaluated separately.

Cancer – The potential for harm from simultaneous exposure to more than one chemical (chemical mixtures) that may contribute to cancer is also assumed to be additive by regulatory agencies (Health Canada 2004, Williams and Paustenbach 2002). Again, the additive approach treats all chemicals as equal in their ability to cause harm, despite potential differences in the underlying toxicological evidence used (for example, animal versus human data). This process also assumes that intakes of individual chemicals are relatively small, that these chemicals that are mostly similar in their structure, impose biological interactions through similar mechanisms, and/or affect the same targeted organ.

1. For oral exposure to chemicals that may contribute to cancer, the potential for harm for these conditions can be evaluated by summing the incremental lifetime cancer risk (or ILCR) for the individual chemicals:

$$\sum ILCR = ILCR_1 + ILCR_2 + \ldots + ILCR_i$$

Where $ILCR_i$ = Incremental lifetime cancer risk for the i^{th} chemical.

2. For oral exposure to chemicals that may contribute to cancer, the potential for harm for these conditions can also be evaluated by estimating and summing Exposure Ratios for the individual chemicals based on the risk-specific dose (RsD) approach:

$$\sum ER = ER_1 + ER_2 + \ldots + ER_i$$

Where ER_i = Exposure Ratio for the i^{th} chemical.

3. For inhalation exposure to chemicals that may contribute to cancer, the potential for harm for these conditions can be evaluated by estimating and summing Exposure Ratios for the individual chemicals based on the risk-specific concentration (RsC) approach:

$$\sum ER = ER_1 + ER_2 + \ldots + ER_i$$

Where ER_i = Exposure Ratio for the i^{th} chemical.

Combining Exposure Pathways

Combining risk descriptions across exposure pathways is more complex than for a single pathway because there are several points that need to be considered. There are two steps to determine whether two or more exposure pathways should be combined (Williams and Paustenbach 2002):

- identify reasonable exposure pathway combinations
- examine whether it makes sense that the same receptors would consistently face the same type of exposures by more than one pathway

The first step is straight-forward. To combine certain pathways, the same receptor or receptor groups should be exposed to these pathways. If the pathways do not affect the same receptor or receptor groups, these pathways should not be combined. Furthermore, each pathway should be affecting the receptor or receptor groups in the same area and during the same time period because exposures might not occur in other locations or time periods (Williams and Paustenbach 2002).

During the second step, although some pathways may be combined, the same receptor or receptor groups may or may not experience the same type of exposures over the same period of time. Thus, an explanation should be provided for why more than one pathway would apply to the same receptors.

Noncancer endpoints – The potential for harm from simultaneous exposure to chemical mixtures that may contribute to noncancer effects through multiple pathways is assumed to be additive by regulatory agencies based on policies designed not to possibly underestimate risk (Williams and Paustenbach 2002). Specifically, the potential for harm for these conditions can be evaluated by summing the Exposure Ratios for the individual pathways:

$$\sum ER = ER_{\text{exposure pathway 1}} + ER_{\text{exposure pathway 2}} + \ldots + ER_{\text{exposure pathway i}}$$

Where $ER_{\text{exposure pathway i}}$ = Exposure Ratio for the i^{th} pathway.

Short-term (acute) or long-term (chronic) exposure scenarios are evaluated separately.

Cancer – The potential for harm from simultaneous exposure to chemical mixtures that may contribute to cancer through multiple pathways is also assumed to be additive by regulatory agencies based on policies not to possibly underestimate risk (Williams and Paustenbach 2002). Again, the additive approach treats all chemicals as equal in their ability to cause harm, despite potential differences in the underlying toxicological evidence used (for example, animal versus human data). This process assumes that intakes of individual chemicals through each pathway are relatively small, that these chemicals that are mostly similar in their structure, impose biological interactions through similar mechanisms, and/or affect the same targeted organ.

1. For oral exposure to chemical mixtures that may contribute to cancer, the potential for harm for these conditions can be evaluated by estimating and summing incremental lifetime cancer risks (or ILCR) for the individual exposure pathways:

   $$\sum ILCR = ILCR_{\text{exposure pathway 1}} + ILCR_{\text{exposure pathway 2}} + \ldots + ILCR_{\text{exposure pathway i}}$$

   Where $ILCR_i$ = Incremental lifetime cancer risk for the i^{th} exposure pathway.

2. For oral exposure to chemical mixtures, the potential for harm for these conditions can also be evaluated by estimating and summing Exposure Ratios for the individual exposure pathways based on the risk-specific dose (RsD):

   $$\sum ER = ER_{\text{exposure pathway 1}} + ER_{\text{exposure pathway 2}} + \ldots + ER_{\text{exposure pathway i}}$$

   Where $ER_{\text{exposure pathway i}}$ = Exposure Ratio for the i^{th} pathway.

3. For inhalation exposure to chemical mixtures, the potential for harm for these conditions can be evaluated by estimating and summing Exposure Ratios for the individual exposure pathways based on the risk-specific concentration (RsC):

   $$\sum ER = ER_{\text{exposure pathway 1}} + ER_{\text{exposure pathway 2}} + \ldots + ER_{\text{exposure pathway i}}$$

   Where $ER_{\text{exposure pathway i}}$ = Exposure Ratio for the i^{th} pathway.