TASK 3A-1: TOXICOLOGICAL RISK ASSESSMENT PERTAINING TO POTENTIAL OCCUPATIONAL AND RELATED EXPOSURES ASSOCIATED WITH HERBICIDE SPRAYING OPERATIONS AT CFB GAGETOWN – TIER 1 – 1966-67 U.S. TRIALS – MANUFACTURING IMPURITIES (CONTAMINANTS)

- FINAL REPORT -

The Contents Of This Report Encompass Task 3A-1, Tier 1 Portion Of:

"Investigation of Potential Health Effects from The Use of Herbicides and any Herbicide-Related Contaminants, Particularly Dioxins Used at CFB Gagetown From 1952 to the Present"

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ACRONYMS AND ABBREVIATIONS

2,4,5-T	2,4,5-Trichlorophenoxy Acetic Acid
2,4-D	2,4-Dichlorophenoxyacetic Acid
ACGIH	American Conference of Government and Industrial Hygienists
ADI	Acceptable Daily Intake
AhR	Aryl Hydrocarbon Receptor
AI	Active Ingredient
AO	Agent Orange (equal volumes of concentrated *n*-butyl esters of 2,4-dichlorophenoxyacetic acid and 2,4,5-T herbicides)
AP	Agent Purple (*n*-Butyl ester (30%) and *iso*-Butyl ester (20%) of 2,4,5-T and *n*-Butyl ester of 2,4-D)
ATSDR	U.S. Agency for Toxic Substances and Disease Registry
BB_{TRV}	Body Burden TRV
bw	body weight
CDC	U.S. Center for Disease Control and Prevention
CEPA	Canadian Environmental Protection Act
CFB	Canadian Forces Base
COC	Chemicals of Concern
CPF	Cancer Potency Factor
DLC	Dioxin-like compounds (includes PCDDs, PCDFs and PCBs)
DND	Department of National Defence
dw	dry weight
EC	Environment Canada
EDI	Estimated Daily Intake
ED	Exposure Duration
EF	Exposure Frequency
EPC	Exposure Point Concentration
FAO	Food and Agriculture Organization of the United Nations
fg	femtograms = 0.001 pg
gal	gallon (US); equivalent to 3.8 L
HCB	Hexachlorobenzene
HQ	Hazard Quotient
IARC	International Agency for Research on Cancer
I-TEQ	TEQ based on the NATO International TEF scheme ($NATO_{89}$)
ILCR	Incremental Lifetime Cancer Risk Level
JECFA	Joint FAO/WHO Expert Committee on Food Additives
kg bw	kilograms body weight
lb	pounds; equivalent to 0.45 kg
LOAEL	Lowest Observed Adverse effect Level
µg	microgram; 1,000 ng; 1,000,000 pg; 0.001 mg; 0.000001 g
MRL	Minimal Risk Level
ng	nanogram = 1000 pg
NTP	National Toxicology Program
NOAEL	No observed adverse effect level
PBPK	Physiologically based pharmacokinetics
PCBs	Polychlorinated biphenyls
PCDDs	Polychlorinated Dibenzodioxins

PCDFs	Polychlorinated Dibenzofurans
PCP	Pentachlorophenol
pg	picogram; 0.001 ng; 0.000001 µg; 0.000000001 mg; 0.00000000001 g
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppm, m:m	parts per million on a mass to mass basis; equivalent to µg/g
RfD	Reference Dose; equivalent to ADI and TDI
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin; 2,3,7,8-TCDD; T_4CDD
TDI	Tolerable Daily Intake
TEF	Toxic Equivalency Factor
TEQ	Toxic Equivalent Concentration; based on the WHO_{98} TEFs for all DLC unless otherwise noted
TEQ_{DF}	TEQ based on TEFs for dioxins and furans only
TRV	Toxicity Reference Value
UE	Unit Exposure values (from PHED)
U.S. EPA	United States Environmental Protection Agency
WHO	World Health Organization

TASK 3A-1: TOXICOLOGICAL RISK ASSESSMENT PERTAINING TO POTENTIAL OCCUPATIONAL AND RELATED EXPOSURES ASSOCIATED WITH HERBICIDE SPRAYING OPERATIONS AT CFB GAGETOWN – TIER 1 – 1966-67 U.S. TRIALS – MANUFACTURING IMPURITIES (CONTAMINANTS)

EXECUTIVE SUMMARY

ES-1.0 INTRODUCTION

The Government of Canada has committed to identifying and reporting on facts surrounding the use of Agent Orange and Agent Purple during June, 1966, and June, 1967, in addition to the use of other herbicides, sprayed at Canadian Forces Base (CFB) Gagetown between 1952 and present day. As part of this commitment, the Government of Canada has engaged non-governmental experts to assess the possibility military and civilian personnel exposure to herbicides and contaminants within these herbicides, the potential herbicide and contaminant dose received by these personnel and the potential of these herbicides and contaminants to cause harm. Cantox Environmental Inc. was retained to conduct a human health risk assessment to estimate potential exposures, characterize potential health risks, and determine, in an objective manner, whether exposures to herbicides, and associated contaminants, used at CFB Gagetown may be associated with potential human health risks.

The assessment of exposures and related risks arising from Agent Orange, Agent Purple, other herbicides and any herbicide-related contaminants, particularly dioxins, sprayed at CFB Gagetown from 1952 to the present, has been prioritized into three tiers:

- Tier 1 – 1966-67 U.S. Trials - Manufacturing Impurities (contaminants);
- Tier 2 - 1956-2004 - Manufacturing Impurities (contaminants); and,
- Tier 3 - 1956-2004 - All Herbicide Products.

The subject of this report is Tier 1. Tiers 2 and 3 will be the subject of subsequent reports.

ES-2.0 DESCRIPTION OF TIER 1

In March, 1965 the Canadian Ministry of Defence offered the Crops Division of the United States Department of the Army the use of large areas of densely forested land at CFB Gagetown for the purpose of testing defoliant chemicals. The two areas of CFB Gagetown that were affected by this herbicide application in 1966 and 1967 are shown on the map below (Figure ES-1). The test site used in 1966 was approximately 360 metres (1,200 feet) wide by 6.4 kilometres (4 miles) long. A total of eight enlisted men and three Officers (the Commanding Officer, a Range Officer and a co-pilot) from the Canadian Military were listed as participating in the project. This information is not available for 1967. Herbicides were applied from a helicopter.

The focus of the Tier 1 report is the contaminants present in some herbicide products applied at CFB Gagetown in the U.S. trials in 1966 and 1967, specifically:

1. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD; 2,3,7,8-TCDD; dioxin) present in 2,4,5-T (a component of Agent Orange and Agent Purple and an unregistered mixture that contained 2,4,5-T in acid form);

2. Hexachlorobenzene (HCB) present as a contaminant in picloram (Tordon formulations Tordon 22K and Tordon 101);

3. One herbicide formulation (M-2993) contained both 2,4,5-T (contaminated with TCDD) and picloram (contaminated with HCB); and,

4. One herbicide preparation that was applied only in 1967 included polychlorinated dibenzo-*p*-dioxins (PCDDs) and furans (PCDFs) in pentachlorophenol (PCP).

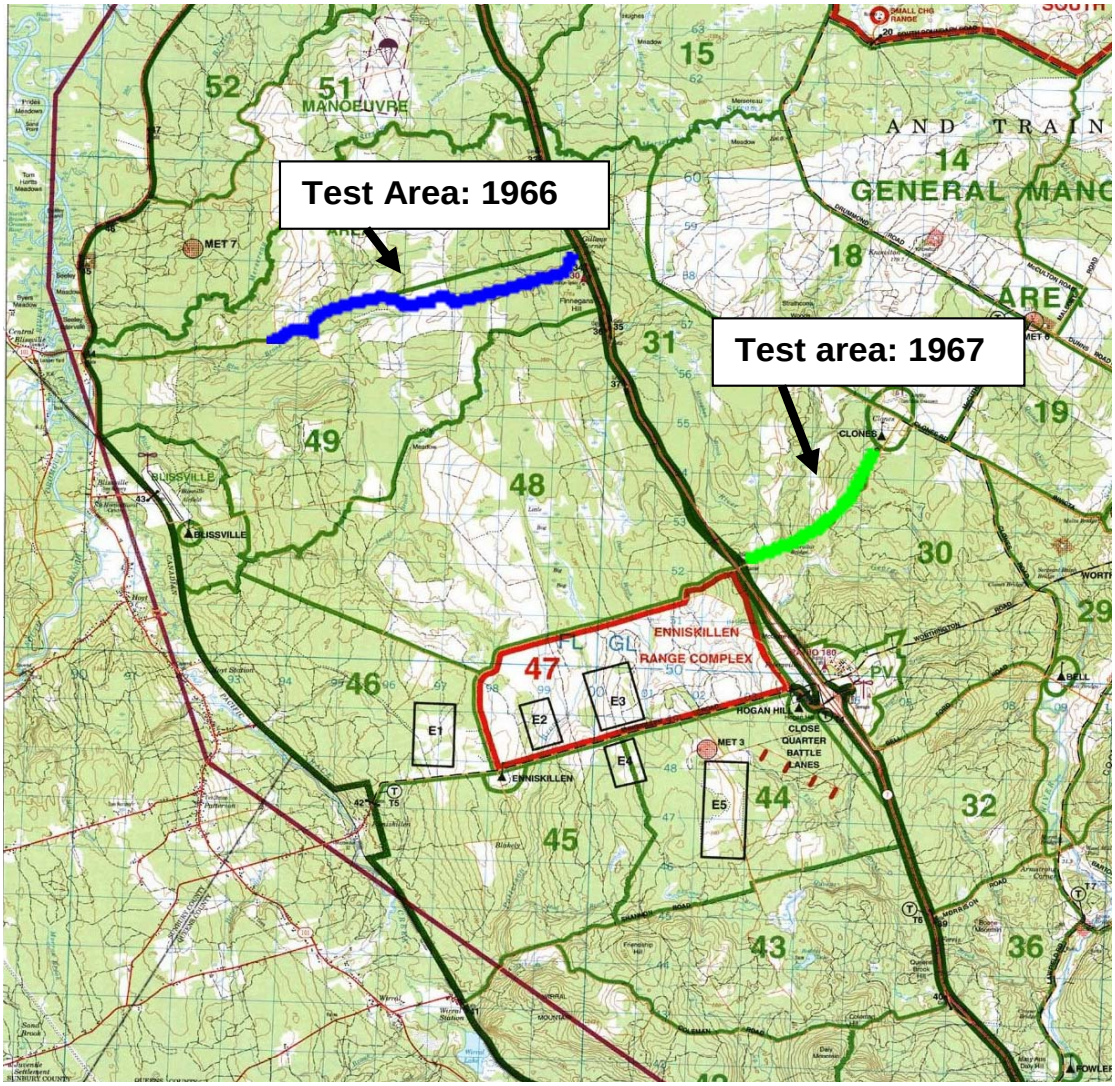


Figure ES-1 Map Section of CFB Gagetown Showing Areas of Herbicide Application for 1966 (shown in blue) or for 1967 (shown in green)

ES-3.0 HEALTH RISK ASSESSMENT METHODOLOGY

Human health risk assessment is a science based tool used to evaluate the potential for adverse human health effects following exposure to chemicals. The "dose-response" principle of toxicology is fundamental to an understanding of the health risks presented by chemicals. All chemicals possess intrinsic toxicity, which is defined as the ability to cause injury to living systems. However, whether or not injury is realized depends on the amount of the chemical that reaches the living system. In the absence of exposure, no injury will occur. As exposure mounts, the likelihood of injury increases.

Based on this principle, it is generally accepted that the two primary determinants of chemical-based health risks are the level of ***exposure*** received and the intrinsic ***toxicity*** of the chemical. The principles are often reduced to the simple equation:

RISK = EXPOSURE x TOXICITY

An understanding of these two determinants is critical to the assessment of the health and environmental risks presented by a chemical. Human health risk assessment are conducted using risk assessment procedures which have been developed by regulatory agencies such as Health Canada and the United States Environmental Protection Agency (U.S. EPA). The human health risk assessment followed the four standard steps of any risk assessment (see Figure ES-2).

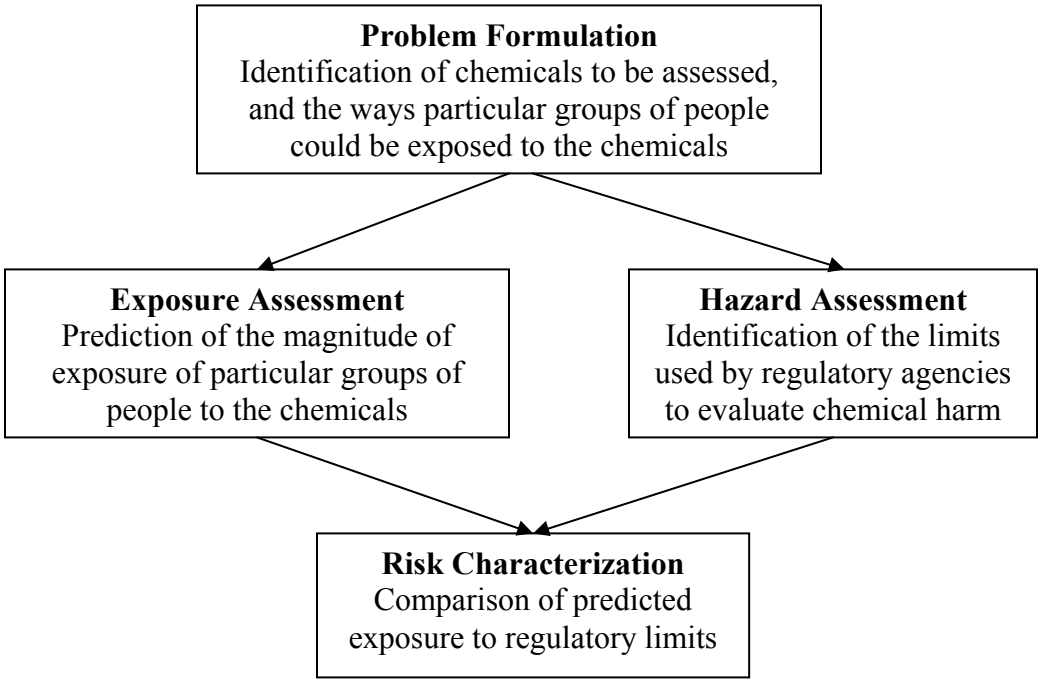


Figure ES-2 The Basic Steps of a Risk Assessment

The chemicals discussed in this report have been linked to both cancer and other non-cancer effects. Risks that link chemical exposure and cancer are calculated differently from other non-cancer health risks that are known to be associated with that chemical. In the case of chemicals that do not cause cancer, the level of risk is determined using the ratio of exposure to the level

associated with no harm. A ratio less than or equal to 1 is considered to be "acceptable", and indicates that the exposure level does not exceed the safe level or benchmark. In the case of chemicals believed to cause cancer in people, the level of risk experienced after an exposure to a chemical is linked to the possibility that a person could develop cancer sometime during his/her lifetime. The definition of acceptable risk varies among countries or other organizations. Health Canada qualifies the development of an additional cancer in one person out of 100,000 people (*i.e.*, 0.00001) as "*de minimus*" or "essentially negligible". Furthermore, Health Canada views a range of one cancer in 100,000 to one cancer in 1,000,000 as a minimally desirable target, depending on the specific situation and on the degree of conservatism and uncertainty in the risk assessment. A third approach for assessing risks was included in the current human health assessment. For chemicals like dioxin, that are persistent within the body, there is a potential for very high short-term exposures to remain in the body and result in long-term health effects. A body burden based approach was also used to evaluate the potential health risk associated with dioxin exposures.

ES-4.0 PROBLEM FORMULATION

Problem formulation is the information gathering step where the chemicals, receptors (people) and pathways (the ways particular groups of people could be exposed to the chemicals) which need to be assessed are identified. For the Tier 1 risk assessment of the 1966-67 U.S. trials, the chemicals of concern are the manufacturing impurities (contaminants) of the herbicides applied during these trials. These contaminants include PCDD/PCDF (dioxins) and hexachlorobenzene (HCB).

The risk assessment does not evaluate risks to particular people. Rather, risks are assessed for representative groups of people. The following groups of people were assessed:

1. Mixer/Loader – These individuals were responsible for handling, mixing and loading the various herbicide products. For the 1966-67 scenario, this group only included military personnel and it was assumed that different individuals were involved in each year. Exposures of the mixer/loader was assumed to occur during routine mixing and loading activities through the inhalation of vapours and dermal absorption through skin. An accidental scenario was also evaluated in which the mixer/loader experiences an additional dermal exposure event as a result of a spill of concentrated herbicide.

2. Applicator – These individuals are the pilots responsible for applying the herbicide products. For the 1966-67 scenario, this group only included military personnel. It was assumed that all herbicide active ingredients were in liquid form and that exposure occurred as a result of absorption through both dermal and inhalation routes.

3. Flagger – The 1966 and 1967 aerial spray campaigns involved a number of individuals on the ground whose job was to assist the aerial applicator by marking specific locations to begin and end specific spraying events. A flagger was the individual that was responsible for marking the beginning or end of a plot targeted for the aerial application of herbicides. Military personnel were responsible for this activity and it was assumed that an individual was involved in the flagging of all plots receiving chemical mixtures during either the 1966 or 1967 trials. Exposure occurred as a result of absorption through both dermal and inhalation routes.

4. Post-Application Scout – These individuals were responsible for entering the forested area sometime following the application of herbicides for the purpose of making field observations. It was assumed that these receptors would come into direct dermal contact with recently sprayed vegetation. It was assumed that military personnel would be responsible for this activity.

5. On-Site Military Trainee – These military personnel were those who may have spent significant amounts of time in various areas of the base while completing military training, including survival training. It was assumed that this receptor group would have come into direct contact with various environmental media (*i.e.*, soil and wild berries) which have been impacted by the applied herbicide products. For the 1966-67 scenarios, it was assumed that training exercises occurred in direct proximity to the spray areas, during the time of the spraying.

Several receptor groups have not been included in the current assessment (Tier 1). These will be considered in subsequent Tiers. These include:

- Off-Site Civilian – These individuals are those who may have lived near the military base and occasionally used specific areas of the base for recreational purposes (*e.g.*, hunting, walking, berry picking, *etc*.). This receptor group was not considered for the 1966-67 scenarios as these spray areas are fairly small and remote resulting in limited opportunities for exposures. Spray drift modelling has estimated that virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, indicating that off-site drift would not have occurred.

- Civilian Spouses – spouses of military personal may have come into contact with the chemicals through contact with clothing brought home by military personnel following spray activities. These potential receptors were not considered as their exposures would have been small as compared to the military personnel directly involved in the spray activities, and as such, these concerns would be less than those quantitatively evaluated.

Exposure pathways (direct and indirect) and scenarios were developed for the following receptor and exposure situations:

- Mixer/loader – routine
- Applicator – routine
- Flagger – routine
- Post Application Scout – routine
- Military Trainee – routine
- Mixer/loader – accident (spill)
- Flagger/trainee – accident (direct spray)

Exposure pathways considered included direct contact (incidental ingestion and dermal contact), inhalation of vapours, contact with impacted soil and/or foliage following spraying, and ingestion of berries impacted by the spraying.

Several potential exposure pathways were eliminated from further consideration. These included:

- Groundwater – No potable groundwater wells exist in close proximity to the 1966 and 1967 spray areas. Base bivouac wells were installed in the mid-1990's and as such were not relevant to the current assessment. The environmental characteristics of dioxins and HCB preclude the likelihood that either dioxin or HCB would migrate from the spray areas to any potable water well either on the base or in its immediate proximity.

- Surface Water – No significant surface water receptors (those with known recreational uses such as fishing) were identified in the vicinity of the 1966 spray area. The 1967 spray area does lie within the watershed that drains the Nerepis River; however, the area is approximately 5 km from the main channel of the river. In addition, environmental characteristics of dioxins and HCB preclude the likelihood that either chemical would migrate from the spray areas to any surface water bodies either on the base or in its immediate proximity.

- Hunting/fishing - this potential pathway was not considered for the 1966-67 scenario as these spray areas are fairly small and remote resulting in limited opportunities for exposures. Spray drift modelling has estimated that virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, indicating that off-site drift would not have occurred.

- Brush clearing and burning - Brush clearing was not conducted manually in either 1966 or 1967. As such, pathways related to brush clearing and burning were not considered.

- Volatilization following application – given the low vapour pressures of dioxin and HCB this pathway was not considered relevant.

- Contact with chemicals in non-designated spray areas – based on the information provided by the spray drift model which indicated that virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, drift to non-designated spray areas was not considered. Areas immediately adjacent to the spray plots were considered as part of the actual spray plots.

As appropriate, these pathways will be considered for subsequent Tiers of the human health risk assessment.

ES-5.0 EXPOSURE ASSESSMENT

Exposure assessment estimates the magnitude (level) of exposure for the groups of people and chemicals being assessment. A range of exposures to people at CFB Gagetown in 1966-67 was estimated. The high-case estimate employs a series of individual worst-case assumptions, applied one after another, introducing a bias that represent a worst-case. Similarly, the central and low exposure estimates employed, whenever possible, central (average) and low-end exposure assumptions, respectively. A range of potential exposure values (facilitated through the use of selected low, central and high input parameters) were developed to provide a general appreciation for the level of uncertainty and variability present within the quantitative exposure estimates.

All Canadians are exposed to low levels of dioxins and HCB through background sources such as air, water, soil and foods including those purchased from supermarkets. This background exposure occurs as a result of normal activities unrelated to herbicide use at CFB Gagetown.

ES-6.0 HAZARD ASSESSMENT

Hazard assessment evaluates the toxicological potency of the chemicals of concern and establishes 'safe' levels of exposure. Health effects that may result from exposure to the chemicals are also identified. Dioxins and HCB are known to be associated with various health effects which are summarized below (Table ES-1).

Table ES-1 Chemicals of Concern

Chemical	Major Human Health Effects	
	Non-Cancer	Cancer
Hexachlorobenzene (HCB)	Blood (heme production), as well as liver, ovary, central nervous system effects and effects on other organs	Thyroid cancer, liver cancer, soft tissue sarcoma
Dioxins	Reproductive/hormonal disorders; skin disorders, impaired liver and immune system function, central nervous system pathology, and other developmental effects	Generalized excess of all cancers (linked to occupational exposure and industrial accidents) without any pronounced excess at any specific organ or tissue

The risk assessment uses regulatory limits to predict the potential for these health effects to occur. Most regulatory limits are based on animal studies. Epidemiological studies of which relate exposures to the chemicals of concern and resulting health effects were also reviewed. Studies of Vietnam veterans provide direct evidence of possible health effects of Agent Orange exposure. Therefore, where the risk assessment predicts elevated health risks, the epidemiological information from the Vietnam veterans can be used to identify potential health outcomes among affected individuals who were at CFB Gagetown in 1966-67. It is necessary to point out that the illnesses reported among Vietnam veterans are associated with exposure to all the chemicals in all the herbicide preparations (and other chemicals) with which they may have come into contact. This report only deals with two contaminants.

Based on the epidemiological evidence, there is sufficient to limited evidence of an association between exposure to herbicides including Agent Orange, among Vietnam veterans who participated in defoliation and chemical spraying (Operation Ranch Hand), and health outcomes including cancer (several forms including soft tissue sarcoma, non-hodgkin lymphoma, hodgkin disease, chronic lymphocytic leukemia, respiratory cancers, prostate cancer); chloracne; peripheral neuropathy; porphyria cutanea tarda; type 2 diabetes (mellitus); and, spina bifida.

There is inadequate or insufficient evidence of an association with other health outcomes including some forms of cancer (acute myelogenous leukemia; hepatobiliary cancers; oral, nasal/nasopharyngeal cancer; bone and joint cancer; breast cancer; female reproductive cancer (cervix, uterus, ovary); urinary bladder cancer; renal cancer; testicular cancer; leukemia (other than CLL); skin cancers), and other non-cancer outcomes such as abnormal sperm characteristics and infertility; spontaneous abortion; neonatal or infant death and stillbirth in offspring of exposed individuals; low birth-weight in offspring of exposed individuals; birth defects (other than spina bifida) in offspring of exposed individuals; neurobehavioral disorders (cognitive and

neuropsychiatric); movement disorders, including parkinson's disease and amyotrophic lateral sclerosis (ALS); chronic peripheral nervous system disorders; respiratory disorders; gastrointestinal, metabolic, and digestive disorders (changes in liver enzymes, lipid abnormalities, ulcers); immune system disorders (immune suppression, autoimmunity); circulatory disorders; al amyloidosis; endometriosis; and, effects on thyroid homeostasis.

ES-7.0 RISK CHARACTERIZATION AND CONCLUSIONS

Risk characterization compares the results of the exposure assessment and the hazard assessment and attempts to quantify the chance that an adverse health effect (risk) occurred. The mixer/loader, the applicator, the flagger, the field scout, and the flagger or trainees accidentally exposed during herbicide application were all assumed to have experienced short-term exposures which may have resulted in potential short-term (non-cancer only) and long-term (cancer and/or non-cancer) risks. Military trainees were assumed to have long-term exposure which may potentially relate to long-term risks. Risks associated with dioxin and HCB short- and long-term exposures are listed below.

Dioxins

- With the exception of the Applicator scenario, the short-term risk estimates for all acute exposure scenarios (under the central exposure estimate) were greater than a HQ value of 1.0, indicating that the central exposure estimates exceeded the short-term or acute TRV (200 pg TEQ/kg bw/day). A HQ value greater than 1.0 does not indicate that adverse health effects would have occurred; however, it does indicate that some receptors may have experienced elevated exposures and as such, the potential for elevated risks.

- The short-term risks predicted for all routine exposure scenarios have been classified as "less serious" by ATSDR. "Serious" effects were not noted until exposures of more than 300-fold greater than the acute TRV. These "less serious" exposure levels are not indicative of elevated risks of long-term irreversible health effects, rather, the potential for short-term reversible effects, of the nature considered "less serious".

- Risk estimates predicted for the accident scenarios were indicative of potentially 'serious' effects; however, the occurrence of accidents of this nature during the 1966 and 1967 spray periods remains uncertain. While elevated risks do not necessarily equate to certain effects it does raise the level of concern and indicates that further epidemiological investigation of individuals involved in these operations is warranted.

- Long-term or chronic risk estimates for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas more than a year following the spray applications were all less than levels that would be indicative of a concern (HQ < 1); as a result, no dioxin related adverse health risks are predicted for military trainees potentially exposed in this manner.

- Elevated body burden were predicted for the two accident scenarios. Elevated body burdens (*i.e.,* levels above the Body Burden $_{TRV}$) may have persisted in persons experiencing accidental exposures for approximately 52 years following the initial accidental spray/spill event. Background individuals (*i.e.,* those not involved in spraying activities at CFB Gagetown) of the same age were predicted to have dioxin body burden levels above the Body Burden$_{TRV}$ for 17.5 years. In other words, dioxin body burden levels among the general population in the 1960's and 1970's were greater than the levels considered acceptable today.

- The body burden results of this assessment are comparable to estimates for the Ranch Hand Veterans who served in Vietnam.

- Based on this assessment, the current body burden levels of individuals who may have experienced elevated exposures during the 1966/67 trials would not likely be distinguishable from the body burden levels of the general population. Although these individuals may currently have body burden levels similar to those of the general population, these individual likely experienced many years of elevated dioxin body burden levels relative to the general population.

- Further investigations of individuals who were present in the vicinity of the spray applications during 1966 and 1967, and may have been experienced these acute exposure events though accidents similar to those considered herein, is warranted. These further investigations could involve body burden analysis, although as indicated above, 40 years after these exposures the body burdens of people are not likely to be distinguishable from the body burden levels of the general population. Additionally, this further investigation could involve an epidemiological study of exposed individuals wherein the incidence of health effects related to the chemicals of concern is investigated.

Hexachlorobenzene

- Short-term or acute estimates for all acute exposure scenarios, with the exception of the mixer/loader accident scenario, are less than levels that would be indicative of a concern (HQ < 1). HQ estimates marginally exceed the 1.0 benchmark for the high end (worst case) mixer/loader accident scenario only. This exposure scenario is considered highly conservative. Given the marginal exceedances estimated and the highly conservative nature of this evaluation, these exceedances are not considered significant or indicative of a potential health risk.

- Long-term or chronic risk estimates for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas more than a year following the spray applications are all less than levels that are indicative of a concern (HQ < 1 and ILCR < 10^{-5} or 1/100,000); as a result, no HCB related adverse health risks are predicted for military trainees potentially exposed in this manner.

- Lifetime cancer risk estimates for all acute exposure scenarios, with the exception of the mixer/loader accident scenario, are less than levels that are indicative of a concern (ILCR $< 10^{-5}$ or 1/100,000). ILCR estimates marginally exceed the 10^{-5} benchmark for the high end (worst case) mixer/loader accident scenario. ILCR estimates for the central tendency receptor are essential equivalent to the benchmark for the 1967 spray period. These risk estimates assume the potential for an increased cancer risk following a one-hit exposure. The evaluation of cancer risks following acute duration exposures is an area of high uncertainty and questionable relevance. Given the marginal exceedances estimated and the highly conservative nature of this evaluation, these exceedances are not considered significant or indicative of an elevated cancer risk.

ES-8.0 UNCERTAINTIES

Where possible, assumptions and estimations were made to err on the side of caution, that is, to over-predict rather than under-predict potential risks. Uncertainties include those surrounding the identification of the people most at risk, how they are exposed to chemicals, concentrations of chemicals in various environmental media (such as air, soil, vegetation), the selection of appropriate regulatory limits (for example, the long-term regulatory limit for dioxins is based on effects in the off-spring of exposed females, which may not be relevant for military personnel in 1966-67), and the use of a body burden approach to estimate risks.

TASK 3A-1: TOXICOLOGICAL RISK ASSESSMENT PERTAINING TO POTENTIAL OCCUPATIONAL AND RELATED EXPOSURES ASSOCIATED WITH HERBICIDE SPRAYING OPERATIONS AT CFB GAGETOWN – TIER 1 – 1966-67 U.S. TRIALS – MANUFACTURING IMPURITIES (CONTAMINANTS)

1.0 INTRODUCTION

The Government of Canada has committed to identifying and reporting on facts surrounding the use of Agent Orange and Agent Purple during June, 1966 and June, 1967 in addition to the use of other herbicides (and any herbicide-related contaminants) sprayed at CFB Gagetown between 1952 and present day. The Government of Canada is also committed to identifying military and civilian personnel who potentially could have been exposed to Agent Orange, Agent Purple, other herbicides and any herbicide-related contaminants, particularly dioxins, sprayed at CFB Gagetown from 1952 to the present day. The Government will engage non-government experts to determine the degree and impact of potential exposure of both former and current serving Canadian Forces' members and civilian employees of the Department of National Defence (DND) within the relevant parameters of the various fact-finding tasks. This will include assessing the potential of the chemicals to cause harm, the possibility of exposure, and the dose of the potential exposure in all relevant cases. The Government of Canada understands and acknowledges that current and former citizens in the area surrounding CFB Gagetown are concerned about long term and cumulative impacts of the use of these herbicides on the environment and on their health. The Government of Canada will provide an opportunity and means for citizens (as well as current and former CF members and DND civilian employees) to identify themselves and their specific concerns to an external Fact Finding and Outreach Coordinator in the Gagetown area. These issues will be studied and assessed through the fact-finding initiative.

As part of this commitment, the Government has engaged Cantox Environmental Inc. (CEI) to determine the potential for the above mentioned compounds to cause harm to human health, in addition to the probability and degree to which former Canadian Forces' members and civilians might have been exposed to Agent Orange, Agent Purple and other herbicides. CEI is an independent consulting firm with expertise in the field of risk assessment and toxicology, and has been retained to conduct a detailed toxicological risk assessment. The human health risk assessment will be used to estimate potential exposures, characterize potential health risks, and determine, in an objective manner, whether potential exposures to herbicides (as they were used at CFB Gagetown from 1952 to the present) may be associated with potential human health risks.

The "dose-response" principle of toxicology is fundamental to an understanding of the health risks presented by chemicals. All chemicals possess intrinsic toxicity, which is defined as the capacity to cause injury to living systems. However, whether or not the capacity to cause injury is realized depends on the amount of the chemical that reaches the living system (*i.e.*, the level of exposure received). In the absence of exposure, no injury will occur. As exposure mounts, the likelihood of injury increases. With few exceptions, chemicals do not cause any injury below a certain "threshold dose". In other words, exposure must reach a certain level before any toxicity is expressed. What makes certain chemicals more toxic than others is the magnitude of that threshold dose and the severity of health effects that might result from exposure.

Based on this principle, it is generally accepted that the two primary determinants of chemical-based health risks are the level of ***exposure*** received and the intrinsic ***toxicity*** of the chemical. The principles are often reduced to the simple equation:

RISK = EXPOSURE x TOXICITY

An understanding of these two determinants is critical to the assessment of the health and environmental risks presented by a chemical. There is a need to examine the potential for exposure before any risk can be determined because if there is no exposure than can be no risk. The approach adopted to assess the potential risks associated with herbicide use at CFB Gagetown respected the need to examine both determinants.

The assessment of exposures and related risks arising from Agent Orange, Agent Purple, other herbicides and any herbicide-related contaminants, particularly dioxins, sprayed at CFB Gagetown from 1952 to the present has been prioritized into three tiers:

- Tier 1 – 1966-67 U.S. Trials – Manufacturing Impurities (contaminants);
- Tier 2 – 1952-2004 – Manufacturing Impurities (contaminants); and,
- Tier 3 – 1952-2004 – All Herbicide Products.

The subject of this report is Tier 1; Tiers 2 and 3 will be the subject of subsequent reports, and as such, findings and conclusions of the health risk assessment for Tier 1 are presented herein.

This report is organized as follows:

- Section 2.0: Description of Tier 1
- Section 3.0: Health Risk Assessment Methodology
- Section 4.0: Problem Formulation
- Section 5.0: Exposure Assessment
- Section 6.0: Hazard Assessment
- Section 7.0: Risk Characterization
- Section 8.0: Uncertainties
- Section 9.0: Conclusions and Discussion
- Section 10.0: Document Sign-off
- Section 11.0: References

- APPENDIX A Dioxin and Hexachlorobenzene Contaminant Levels in Herbicides Used During the 1966-67 U.S. Herbicide Trials
- APPENDIX B Toxicological Profiles
- APPENDIX C Estimates Of Daily Intakes Of Dioxins And Hcb For The Canadian Population
- APPENDIX D Background Information On The Pesticide Handlers Exposure Database (PHED)
- APPENDIX E Worked Example
- APPENDIX F An Evaluation of Potential Deposit Beneath Flight Lines During Aerial Herbicide Spraying, Base Gagetown, NB 1966-1967 (REMSpC Spray Consulting)

- APPENDIX G Scoping Study To Assess Potential Historical Surface And Groundwater Migration Associated With Herbicide Spraying Operations At Cfb Gagetown (Task 2E) (Jacques Whitford)
- APPENDIX H Peer Review and Health Canada Review Comments and Responses to Comments

1.1 Dioxins

Polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) constitute a group of highly persistent ubiquitous chlorinated organic chemicals. The degree of health risk posed by PCBs and dioxins in the environment remains a subject of controversy despite an extensive database of scientific research, particularly in the case of 2,3,7,8- tetrachlordiobenzo-p-dioxin (TCDD), the most potent dioxin congener. "Dioxins" commonly refers to a group of 75 polychlorinated dibenzo-p-dioxin and 135 polychlorinated dibenzofuran congeners, of which less than 20 are considered biologically active (UK COT, 2001). Chemically, the term PCBs denotes a family of 209 closely-related substances, referred to as congeners, which exhibit a wide range of physical and chemical properties, as well as toxicological potential. Among the 209 PCB congeners, 12 exhibit similar biological activity to PCDDs and PCDFs and are referred to as "dioxin-like PCBs". The structurally related compounds, which all bind to the aryl hydrocarbon receptor (AhR), the ligand-activated transcription factor, are commonly referred to as dioxin-like compounds (DLCs). The toxicity of these substances is further discussed in Section 6.2 and Appendix B.

Because dioxin-like compounds are commonly found in complex mixtures within the environment, WHO and several other regulatory groups have adopted the Toxic Equivalency (TEQ) approach for risk assessment. PCDDs, PCDFs and dioxin-like PCBs have been assigned Toxic Equivalency Factors (TEFs) based on their relative potency as compared to 2,3,7,8-TCDD. TEFs have been developed in relation to TCDD for all dioxin-like compounds that meet the following criteria: a) show a structural relationship to PCDDs/PCDFs, b) bind to the aryl hydrocarbon (Ah) receptor, c) elicit dioxin-specific biochemical and toxic responses; and, d) are persistent and accumulate through the food chain. This approach assumes that the combined toxic effects of each of the individual components of the mixture act in an additive manner, rather than a synergistic or antagonistic manner. The toxicity of TCDD is established as a value of 1, with the toxicity of all other PCDD/PCDFs a fraction of this toxicity. The amount of congener present in a sample is multiplied by its TEF to give the "toxic equivalent" concentration (TEQ) for the congener expressed in terms of 2,3,7,8-TCDD equivalents. The total dioxin TEQ approach and current values have been accepted internationally as the most appropriate way to estimate the potential health risks of dioxin mixtures (Schecter *et al.*, 2006).

Several TEF schemes have been developed (Table 1-1). Currently, the WHO_{98} scheme is the approach preferred by regulatory agencies internationally. Unless noted otherwise, all TEQs reported in this report utilize the WHO_{98} TEFs.

Table 1-1 Various Toxic Equivalency Factors (TEFs)

		U.S. EPA_{87}	$NATO_{89}$	WHO_{94}	WHO_{98}
Dioxins (PCDDs)	2,3,7,8-TCDD	1	1		1
	1,2,3,7,8-PCDD	0.5	0.5		1
	1,2,3,4,7,8-HCDD	0.04	0.1		0.1
	1,2,3,6,7,8-HCDD	0.04	0.1		0.1
	1,2,3,7,8,9-HCDD	0.04	0.1		0.1
	1,2,3,4,6,7,8-Hepta CDD	0.001	0.1		0.01
	OCDD	0	0.001		0.0001
Dibenzofurans (PCDFs)	2,3,7,8-TCDF	0.1	0.1		0.1
	1,2,3,7,8-PCDF	0.1	0.05		0.05
	2,3,4,7,8-PCDF	0.1	0.5		0.5
	1,2,3,4,7,8-Hexa CDF	0.01	0.1		0.1
	1,2,3,6,7,8-Hexa CDF	0.01	0.1		0.1
	1,2,3,7,8,9-Hexa CDF	0.01	0.1		0.1
	2,3,4,6,7,8-Hexa CDF	0.01	0.1		0.1
	1,2,3,4,6,7,8-Hepta CDF	0.001	0.01		0.01
	1,2,3,4,7,8,9-Hepta CDF	0.001	0.01		0.01
	OCDF	0	0.001		0.0001
PCBs	3,3',4,4'-TCB (#77)			0.0005	0.0001
	3,4,4',5-TCB (#81)			-	0.0001
	2,3,3',4,4'-PeCB (#105)			0.0001	0.0001
	2,3,4,4',5-PeCB (#114)			0.0005	0.0005
	2,3',4,4',5-PeCB (#118)			0.0001	0.0001
	2',3,4,4',5- PeCB (#123)			0.0001	0.0001
	3,3',4,4',5- PeCB (#126)			0.1	0.1
	2,3,3',4,4',5-HxCB (#156)			0.0005	0.0005
	2,3,3',4,4',5'-HxCB (#157)			0.0005	0.0005
	2,3',4,4',5,5'-HxCB(#167)			0.00001	0.00001
	3,3',4,4',5,5'- HxCB (#169)			0.01	0.01
	2,2',3,3',4,4',5-HpCB(#170)			0.0001	-
	2,2',3',4,4',5,5'- HpCB (#180)			0.00001	-
	2,3,3',4,4',5,5'-HpCB(#189)			0.0001	0.0001

Adapted from U.S. EPA (2003)

- U.S. EPA_{87} – U.S. EPA (1987)
- $NATO_{89}$ – NATO/CCMS (1988)
- WHO_{94} – Ahlborg *et al*. (1994)
- WHO_{98} – van den Berg *et al*., 1998)

$NATO_{89}$ is commonly referred to as the NATO International TEF Scheme (I-TEQ)

2.0 DESCRIPTION OF TIER 1

In March, 1965 the Canadian Ministry of Defence offered Crops Division of the Department of the Army of the United States the use of large areas of densely forested land at CFB Gagetown for the purpose of testing defoliant chemicals then under testing for use in Southeast Asia (Demaree and Creager, 1968). A test site that contained a mix of conifers and deciduous broadleaf species was selected for carrying out this experimental test program. It was determined that this dense, undisturbed forest cover was similar to vegetation densities encountered in temperate and tropical areas of Southeast Asia. This suggests that data regarding important factors such as rates of application and deposition that have been developed for exposure models used for Vietnam (Stellman and Stellman, 2004) were similar to the experimental applications of herbicide at CFB Gagetown. This data can be used where data specific to activities at CFB Gagetown are lacking.

The tests occurred over a few days during the two year period, with separate areas tested in 1966 and 1967. The two areas of CFB Gagetown that were affected by herbicide application in 1966 and 1967 are shown on the map below (Figure 2-1).

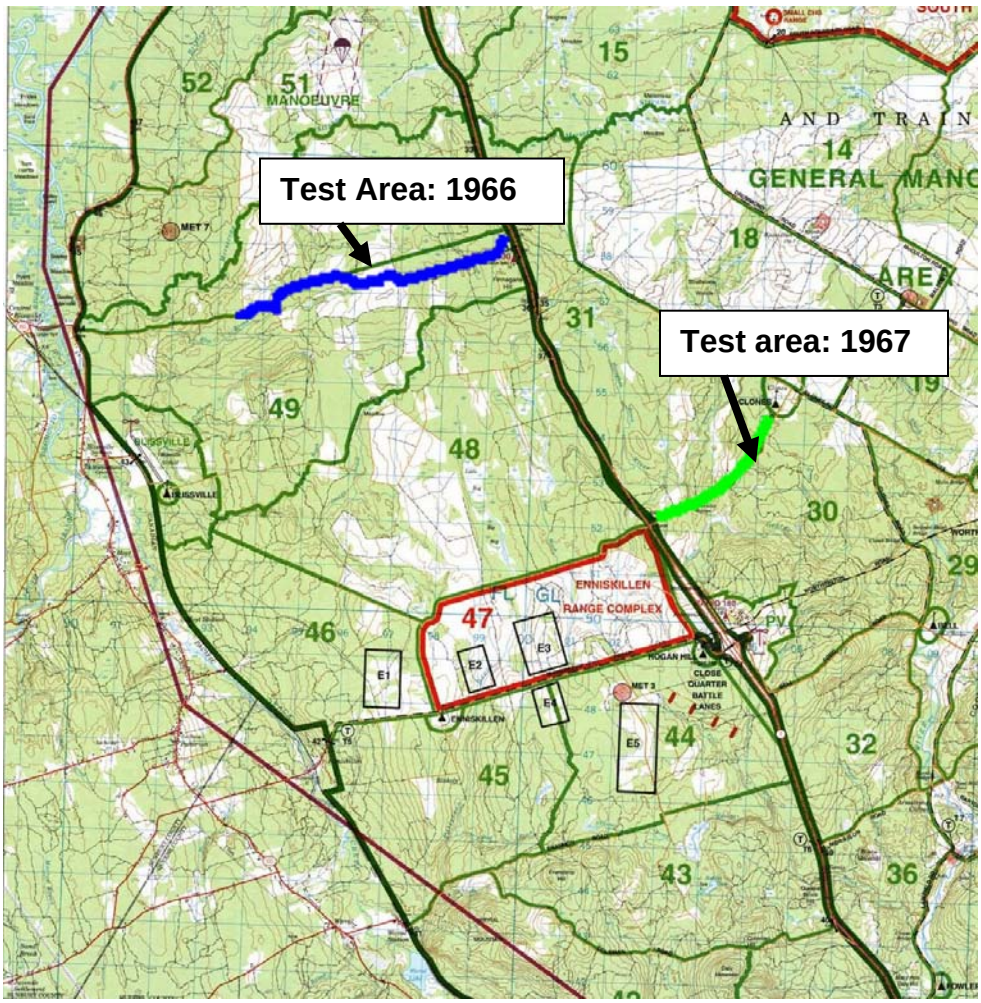


Figure 2-1 Map Section of CFB Gagetown Showing Area of Herbicide Application for 1966 (shown in blue) and for 1967 (shown in green)

The test area used in 1966

The test site at CFB Gagetown that was used in 1966 was approximately 360 m (1,200 ft) wide by 6.4 km (4 miles) long. The height of vegetation ranged from 6 to 22.5 m (20 to 75 ft). The terrain was difficult to navigate, and could only be accessed along an east to west oriented path by tracked vehicles. Clearly it was not easy for an individual on foot to move quickly from one part of the test area (characterized as 'mud and mire' by Demaree and Creager (1968)) to another. A total of eight enlisted men and three Officers (the Commanding Officer, a Range Officer and a co-pilot) from the Canadian Military were listed as participating in the project (Demaree *et al.*, 1966).

A total of 116 plots were prepared for the test applications of herbicides of various kinds. Ten of the 116 plots received no herbicide of any kind. Each plot was 200 ft by 600 ft wide (60 m x 180 m) and plots were separated by from one another by a 100 ft buffer zone. Each plot was 2.75 acres (1.1 hectare) in area. These were established on either side of the access trail with fifty-two plots on the north side and sixty-four to the south (the width of the access buffer strip was not specified but can also be presumed to be 100 ft (30 m). The corners of each plot were marked and one corner was identified by the plot number.

Application method used in 1966

A helicopter was used for all test applications. Sorties (missions) were flown from a small airstrip located outside Blissville, NB, approximately 2 to 4 miles from the test area.

All herbicides were applied from a U.S. Army helicopter supplied for the tests. The spray apparatus consisted of a boom that extended 25 ft either side of the helicopter, an electric pump and a 200-gallon holding tank. Spray nozzles were located at intervals of six inches along the boom (fifteen in total per boom). Delivery of herbicide for application was metered *via* the nozzles which were designed to deliver a specified size of droplet at a specified rate (Note: The rate of application could not be changed for the entire operation. Variation in concentration of the herbicide applied to each test plot was achieved by dilution of herbicide loaded into the tank aboard the helicopter or by repeated passes). The aircraft flew at a speed of 65 knots at treetop level (~15 feet over the canopy). Each concentration of herbicide was applied in duplicate to pairs of plots that were well separated geographically, and each plot received a series of four passes (50 ft x 4 = 200 ft per plot) to complete coverage (Demaree and Creager, 1968).

Plots were flagged at each corner to orient the pilot and the flagman stood on the trail halfway between plot markers. Flags were on extensible poles approximately 50 ft in height. In the event that the flag did not reach the surface of the canopy (was not visible from the air) a smoke signal was used. A system of time runs were used during application such that activation of the spray equipment was initiated at the flag and terminated after the number of seconds of flying time equal to the six hundred feet of test plot length (Demaree and Creager, 1968).

Accuracy of application was an important goal of the project. The same pilot was used throughout this test process to minimize variability. However, it might be expected that on some occasions the flagger on the ground received direct exposure to spray delivered at very low level (~90 ft). In addition for some runs in which 2 or three gallons per acre was applied double (8) or triple (12) the number of passes was required to complete the required coverage with herbicide.

Spray applications took place over a thirty hour period, from daylight to dark on June 14th, 15th and 16th , 1966. According to Demaree and Creager (1968), weather conditions during spraying was influenced by a low pressure atmospheric condition resulting in little or no wind. Some rainfall was noted over the three day period (Last *et al*., 1981).

The test area used in 1967

In 1967 thirty-seven (37) plots located on Rippon Road, east of Broad Road in the area of CFB Gagetown situated approximately ten miles (16 km) from the borders of the base were sprayed. Each plot measured 200 ft by 660 ft (3.0 acres) or slightly larger than plots from 1966. Plots were treated in duplicate but at a fixed volume of 3 gallons per acre (Demaree and Haws, 1968).

Unlike the report prepared for 1966, in 1967 no indication or record was kept to show which of the test plots received a particular herbicide preparation (Demaree and Haws, 1968). For the purposes of this assessment, plots located on either side of the road were deemed duplicates. Each plot received exactly the same measured volume of herbicide (no multiple passes were reported).

Application method used in 1967

Plots were sprayed using a civilian helicopter. The aircraft again performed time and distance flights to deliver the fixed amount of herbicide across the area of the plot. The aircraft flew at forty knots (40 kn) at treetop height.

Plots were flagged only at the corners adjacent to the road. The bush on either side of Rippon Road was characterized as very dense and impenetrable (Demaree and Haws, 1968). Other conditions of spray application were analogous to the tests carried out in 1966. The 1967 tests occurred between June 21st and 24th, 1967. Demaree and Haws (1968) reported unfavourable weather conditions during spraying; however, no details were provided.

Herbicide applications from 1966 and 1967 addressed in this report

The focus of this report is on the contaminants present in some herbicide products applied at CFB Gagetown in the U.S. trials in 1966 and 1967. The chemicals of concern addressed in this report are:

1. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD), present in various forms of 2,4,5-T, which were components of Agent Orange and Agent Purple and an unregistered mixture that contained 2,4,5-T in acid form. At the time of application, there was no discernible contamination of 2,4-D by PCDDs or PCDFs;
2. A second contaminant of concern was hexachlorobenzene (HCB) present as a contaminant in picloram (Tordon formulations Tordon 22K and Tordon 101);
3. One herbicide formulation (M-2993) contained both 2,4,5-T (contaminated with TCDD) and picloram (contaminated with HCB); and,
4. A third group of contaminants present in one herbicide preparation that was applied (only in 1967) was PCDDs and PCDFs in pentachlorophenol (PCP).

The following Table (2-1) contains a summary of herbicide applications that occurred in 1966 and 1967. Only those herbicide products known to have been contaminated with either dioxins or HCB have been included. Other active ingredients will be addressed as part of the Tier 3 risk assessment. Information related to application rates has been obtained from Demaree and Creager (1968) and Demaree *et al.*, (1966) for 1966 and Demaree and Haws (1968) for 1967.

Table 2-1 Summary of Herbicide Application in 1966 and 1967

Herbicide Product	# of Plots	Application Rate (herbicide product)		
		gallons/acre	pounds/acre	g/m^2
1966				
Agent Purple (no diluent)	2	1	10.5	1.18
	2	2	21.0	2.35
	2	3	31.5	3.53
Agent Purple (1:1 dilution)	2	1	5.25	0.59
	2	2	10.5	1.18
	2	3	15.75	2.35
Agent Purple (1:2 dilution)	2	3	10.5	1.18
Agent Orange (no diluent)	2	1	10.5	1.18
	2	2	21.0	2.35
	2	3	31.5	3.53
Agent Orange (1:1 dilution)	2	1	5.25	0.59
	2	2	10.5	1.18
	2	3	15.75	2.35
Agent Orange (1:2 dilution)	2	3	10.5	1.18
70% 2,4-D & 30% 2,4,5-T	2	1	10.5 (combined)	1.18
(no diluent)	2	2	21.0	2.35
	2	3	31.5	3.53
70% 2,4-D & 30% 2,4,5-T	2	1	5.25 (combined)	0.59
(1:1 dilution)	2	2	10.5	1.18
	2	3	15.75	2.35
Agent White (Tordon 101)	4	1	0.27 (picloram)	0.03
(1:1 dilution)	4	2	0.54	0.06
Tordon 22K (1:1 dilution)	4	1	1	0.11
	4	2	2	0.22
	4	3	3	0.33
Tordon 22K (1:3 dilution)	2	1	0.5	0.06
M-2993	2	1	0.5 (picloram)	0.055
(picloram & 2,4,5-T)	2		2.0 (2,4,5-T)	0.11
(1:1 dilution)		2	1.0 (picloram)	0.22
			4.0 (2,4,5-T)	0.44
M-2993	2	2	0.66 (picloram)	0.073
(picloram & 2,4,5-T)			2.66 (2,4,5-T)	0.29
(1:2 dilution)				
1967				
Agent Orange	3	3	26	2.91
Timbertox (pentachlorophenol)	2	3	12	1.35
HCA + 2,4,5-T	2	3	6	0.67
Tordon 22K	6	3	2	0.22
	4	3	3	0.34
	4	3	4.5	0.5
M-3142 (picloram ester)	2	3	6	0.67
Agent White (Tordon 101)	2	3	1.6	0.18

Agent Orange: Equal volumes of concentrated *n*-butyl esters of 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-T herbicides. No 2,4,5-T that was manufactured later than 1970.
Agent Purple: both *n*-Butyl ester (30%) and *iso*-Butyl ester (20%) of 2,4,5-T and the *n*-Butyl ester of 2,4-D. Initially formulated in 1953.
Agent White [Tordon 101]: 1:4 mixture of triisopropanolamine salt of picloram (4-amino-3,5,6-trichloropicolinic acid and 2,4-D.

Appendix A provides details related to the levels of contaminants in the herbicide products used in 1966 and 1967. Appendix A1 provides details related to dioxin contamination and Appendix A2 provides details related to HCB contaminant levels. This information is also summarized in Tables 2-2 and 2-3.

For the purposes of the current assessment all Agent Purple was assumed to be contaminated at levels ranging from 17 to 45 ug TCDD/g AP (ppm TCDD mass:mass) (average of 33 µg/g). All Agent Orange was assumed to have levels of contamination by TCDD ranging between 0.02 and 15 ug TCDD/g AO (average of 2 µg/g). For all other products that contain 2,4,5-T, as the phenoxy acetic acid, the level of contamination by TCDD was assumed to be similar as for Agent Orange. Contaminant levels in PCP ranged from 2.2 to 45 ug TEQ/g PCP (mean value of 9.2 ug TEQ/g PCP). The HCB content in Picloram was determined to be 200 ug HCB/g Picloram (ppm mass:mass).

Table 2-2 Contaminants in Herbicides Applied to Test plots in 1966 (66 of 116 plots)

Number of Plots	Herbicide	Contaminant	Contaminant Concentration (µg/g; ppm mass:mass)		
			Low	Central (mean)	High
1966					
14	Agent Orange containing 2,4,5-T butyl ester	TCDD	0.02	2	15
14	Agent Purple containing 2,4,5-T isobutyl ester	TCDD	17	33	45
12	Other herbicides containing 2,4,5-T acid	TCDD	0.02	2	15
6	M-2993 (picloram and 2,4,5-T)	TCDD HCB	0.02 200	2 200	15 200
20	Picloram	HCB	200	200	200
40	Diquat or cacodylic acid mixtures	--	--	--	--
10	Not sprayed	--	--	--	--

Table 2-3 Contaminants in Herbicides Applied to Test Plots in 1967 (25 of 37 plots)

Number of Plots	Herbicide	Contaminant	Contaminant Concentration (µg/g; ppm mass:mass)		
			Low	Central (mean)	High
1967					
2 (or 3)	Agent Orange containing 2,4,5-T	TCDD	0.02	2	15
2	2,4,5-T	TCDD	0.02	2	15
18	Picloram	HCB	200	200	200
2	Pentachlorophenol (PCP)	PCDDs and PCDFs	2.2 (TEQ)	9.2 (TEQ)	45 (TEQ)
12	Preparations that did not include focus contaminants	--	--	--	--

3.0 HEALTH RISK ASSESSMENT METHODOLOGY

The main components of the risk assessment methodology are outlined in the following figure (see Figure 3-1):

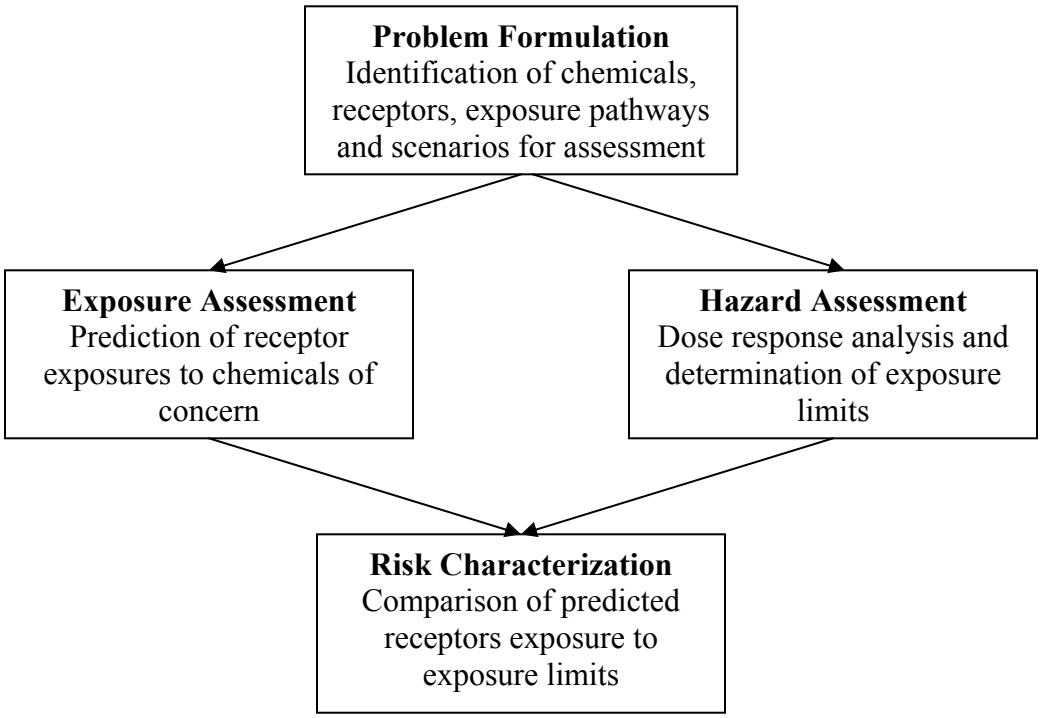


Figure 3-1 The Basic Steps of a Risk Assessment

3.1 Problem Formulation

Problem formulation is an information-gathering and interpretation stage, designed to plan and focus the risk assessment on critical areas of concern for the situation being evaluated. The key tasks requiring evaluation within the problem formulation phase include the following: i) site characterization, which consists of a review of available site data to identify factors affecting the availability of chemicals to potential receptors; ii) chemical characterization, which involves the identification of the chemicals of concern based on site monitoring data; iii) receptor characterization to identify "receptors of concern", which include those with the greatest probability of exposure to chemicals from the site and those that have the greatest sensitivity to these chemicals; and, iv) the identification of exposure pathways, which takes into account chemical-specific parameters, such as mobility, persistence, solubility and volatility, characteristics of the site, such as physical geography, as well as the physiology and behaviour of the receptors.

3.2 Exposure Assessment

The assessment of the potential for adverse effects from chemicals is based on the dose-response concept that is fundamental to the responses of biological systems to chemicals (Filov *et al.*, 1979; Amdur *et al.*, 1991). Because it is not usually practical to measure concentrations of chemicals at the actual site where the adverse response occurs within tissues and cells, these concentrations are estimated based on either the dose of the chemical that actually enters a receptor or more commonly, by the concentrations in various environmental media that act as pathways for exposure. The degree of exposure of receptors to chemicals from the environment therefore depends on the interactions of a number of parameters, including:

- The concentrations of chemicals in various environmental media as determined by the magnitude of point sources as well as background or ambient concentrations;
- The characteristics of the chemicals of concern which affect environmental fate and persistence (*e.g.*, physical-chemical properties);
- The impact of site-specific characteristics, such as local geology, geography and hydrogeology, on chemical behaviour;
- The physiological and behavioural characteristics of the receptors (*e.g.*, respiration rate, soils/dusts intake, time spent at various activities and in different environmental areas); and,
- The various physical, chemical and biological factors that determine the bioavailability (uptake) of chemicals through various exposure pathways.

The primary objective of the exposure assessment was to predict, using a series of conservative assumptions, the rate of exposure (expressed in pg/kg body weight/day or ng/kg body weight/day) of human receptors to the chemicals of concern, through various exposure scenarios and pathways identified in the problem formulation phase.

3.3 Hazard Assessment

The toxic potency of a chemical is dependent upon the inherent toxicity of the chemical itself (*i.e.*, its ability to enact the mechanism of toxicity), as well as the ability of the chemical to reach the site of action (*i.e.*, bioavailability). Toxic potency may be modified by receptor-specific factors such as the ability to resist, repair or adapt to the toxic impact, and depending on the age, sex, species, *etc.*, of the receptor. The dose-response principle is central to the risk assessment methodology, and is characterized for a certain chemical *via* observations of the toxicological effects resulting from experimental exposures of organisms, either in the environment from various point and non-point sources, or in the laboratory under controlled conditions (Doull *et al.*, 1980; FDA, 1982). The development of an exposure limit must incorporate consideration of factors which affect the impact of a given chemical. These factors may be scenario-specific, such as variation in duration or levels of exposure, which may result in impact on different target organs; this requires that the exposure limit is derived from "realistic" exposures representative of those occurring under practical conditions. For many chemicals, the toxic endpoint is also dependent on the route of exposure, as exposure *via* different routes may impact tissues only at the site of entry. In such a case, different exposure limits would be recommended for the different routes of exposure. Similarly, the relative toxic potency of a chemical may vary from one receptor to another (*e.g.*, children are more sensitive than adults to lead toxicity). In these

situations, separate exposure limits for different life stages would be used to ensure protection of sensitive stages of the population.

3.3.1 Derivation of Toxicity Reference Values (TRVs)

For each chemical of concern (COC), a toxicological assessment was conducted, involving identification of mechanism of action and relevant toxic endpoints, and determination of receptor-specific toxicological criteria or toxicity reference values (TRVs). In many cases, chemical-specific assessments have been completed by a regulatory agency (Health Canada or the U.S. Environmental Protection Agency) involving a peer review process. Exposure criteria established by these agencies have been used in the current assessment. These criteria are generally developed for chronic (long-term) exposure situations; the issue of short-term exposures and related risks are discussed separately.

Two basic and quite different methods are commonly recognized by regulatory agencies for the estimation of toxicological criteria for humans and are applied depending on the mode of toxic action of the compound (FDA, 1982; U.S. EPA, 1989). These are the threshold approach (or the no-observed-adverse-effect levels [NOAELs] - extrapolation factor approach) and the non-threshold (or the mathematical model unit risk estimation) approach.

For chemicals with threshold type dose-response relationships (*i.e.*, for which NOAELs can be determined), it is assumed for practical purposes, that there is a threshold of exposure below which the risk of adverse health effects is essentially zero, and no adverse effects will occur. This threshold is commonly referred to as a tolerable daily intake (TDI), reference dose (RfD), or allowable daily intake (ADI). Conservative estimates of this threshold are based on an experimentally-determined NOAEL, with the application of low-dose extrapolation factors. These factors are also called "safety factors" or "uncertainty factors" (FDA, 1982; U.S. EPA, 1989; Health Canada, 1993), and their magnitude is dependent on the level of confidence in the use of available data as a basis for extrapolation to the exposure scenario of the risk assessment. This confidence is dependent on differences in species and duration of exposure, safety of sensitive species and individuals, and the quality of available data (*i.e.*, the weight-of-evidence of the supporting data).

Where available, route-specific and duration specific TRVs (*e.g.*, inhalation TDIs and oral TDIs; acute and chronic TDIs) are used to characterize the hazard of chemicals. An inhalation TDI is analogous to a tolerable concentration (TC) reported on a μg/kg bw/day basis.

The mathematical model unit risk estimation approach assumes that there would be no risk of the occurrence of adverse effects if the rate of exposure or dose was zero. This approach, generally applied to genotoxic carcinogens, yields an estimate of a cancer slope factor or unit risk cancer potency estimate. The slope factor may be used directly in risk characterization to yield predicted risks of cancer incidence in a population.

The selection of the appropriate method to establish an exposure limit depends on several factors including the characteristics of the relationship between exposure level and adverse response (*i.e.*, the shape of the dose-response curve) and available scientific data on the mechanism(s) through which the chemical produces its adverse response (*i.e.*, does the chemical cause damage to genetic material in cells).

3.4 Risk Characterization

Risk characterization for chemicals with a threshold-type dose-response consists of a comparison between the toxicological criteria (*i.e.*, the rate of exposure that would not produce adverse effects) against the total estimated exposure. This comparison can be expressed as a Hazard Quotient (HQ) and is calculated by dividing the predicted exposure by the toxicological criterion, as indicated in the following equation:

Equation 1

$$Hazard\ Quotient = \frac{Estimated\ Exposure\ (pg/kg\ body\ weight/day)}{Exposure\ Limit\ (pg/kg\ body\ weight/day)}$$

Risk characterization for chemicals with a non-threshold-type dose response (*i.e.,* genotoxic carcinogens) consists of a calculation of the incremental lifetime cancer risk (ILCR), which is defined as the predicted risk of an individual in a population of a given size developing cancer over a lifetime. The ILCR is expressed as a fraction representing the prediction that 1 person *per* ***n*** people would develop cancer, where the magnitude of ***n*** reflects the risks to that population; for example, if the ILCR is 0.1 (representing 1 person *per* 10), the predicted risks of any individual developing cancer would be higher than if the ILCR is 0.001 (1 *per* 1,000). The following equation provides the method whereby the ILCR is calculated:

Equation 2

$$ILCR = Estimated\ Exposure(ng/kg\,bw/day)\,x\,Cancer\ Slope\ Factor\,(ng/kg\,bw/day)^{-1}$$

HQ and ILCR levels are effective tools for expressing potential adverse health effects from exposures to chemicals of concern in that:

- They allow comparisons of potential adverse effects on health between chemicals and different exposure scenarios;
- Potential adverse effects can be estimated from exposures to mixtures of chemicals that act on similar biological systems (e.g., all chemicals that cause liver toxicity, or kidney toxicity, or respiratory tract cancers); and,
- They help simplify the presentation of the results so that the reader may have a clear understanding of the significance of these results, and an appreciation of their significance.

3.4.1 Evaluation of Hazard Quotient and Cancer Risk Levels

If the total exposure to a chemical is equal to or less than the toxicological criterion, then the HQ would be 1.0 or less, and no adverse health effects would be expected. For human exposures to non-carcinogens, the toxicological criteria represent the level of total exposure derived from multi-source and multimedia exposures, which would not result in adverse health effects, regardless of the source or route of exposure. In cases where total exposure has been estimated from both background and site sources, it would be valid to compare the estimated exposure to the entire exposure limit, and an acceptable HQ value would be 1.0.

ILCR levels represent the predicted incremental risk of cancer over a lifetime to an individual member of a population of a given size and are expressed as a risk level. ILCRs are evaluated by comparison to a benchmark risk level that is considered to be acceptable. For example, negligible or *de minimis* cancer risk levels are generally considered to range from $1x10^{-4}$ to $1x10^{-6}$. Health Canada considers $1x10^{-5}$ (1-in-100,000) to represent the *de minimus* or 'essentially negligible' risk level (Health Canada, 2004b). Health Canada has indicated that the negligible impact of a 1-in-100,000 incremental risk level for contaminated site exposures leads to the recommendation that a cancer risk level of 1-in-100,000 (1×10^{-5}) is appropriated when assessing and managing federal sites contaminated with carcinogenic substances.

In cases where the estimated exposures or risks are less than the acceptable level, it can be concluded that no observable adverse health effects would be expected to occur, considering the more sensitive members of the population or the majority of the exposure scenarios considered in the assessment.

HQ and ILCR exceedances above acceptable levels are not necessarily indicative of health effects; rather they are indicated of potential risks, as they may reflect overestimation of risk due to the use of overly conservative estimates (*e.g.,* overestimating exposures through the use of maximum soil ingestion rates). This procedure is followed to ensure that the predicted potential impacts on human health were not under-estimated, but also recognizes the potential magnitude of the conservatism built into the risk estimate.

When predicted exposures or risks are greater than the acceptable level, this may indicate the potential for adverse effects in sensitive individuals or in some of the exposure scenarios considered. In these cases, the evaluation of HQs or ILCRs is extremely important because both the exposure estimation procedures and the toxicological criteria are based on a series of conservative assumptions. A certain level of over-estimation of risk is inherently built into the risk assessment process. For example, in cases where there is considerable uncertainty in the data such as the determination of toxicological criteria for cancer causing chemicals (*e.g.*, arsenic), a conservative dose-response extrapolation model is used to derive the toxicological criterion, to ensure the protection of human health.

3.4.2 Assessment of Short-Term (Acute) Exposures

Regulatory agencies such as Health Canada or the U.S. EPA generally develop toxic reference values (TRVs) that establish safe limits for chronic or long-term (lifetime) exposure substances. These TRVs may be specific for the route of exposure such as dermal, oral ingestion or inhalation. Chronic health effects manifest following repeated low level exposures, often occurring after many months, or even years, of prolonged exposure. Chronic effects include endpoints such as cancer, developmental toxicity, liver or renal damage and other systemic effects.

On the other hand, acute, or short-term effects are the result of exposures following contact with a substance that may occur only once or for a short duration (up to 14 days). Acute risks are those which result in immediate harmful effects. Acute effects include endpoints such as eye irritation, skin irritation, nausea and death in the severest cases. Acute exposures at high concentration or to a particularly potent substance usually result in acute effects. Acute exposure

limits are adopted and/or developed for the purpose of assessing the potential for such acute effects.
In the case of chemicals that resist metabolic elimination and accumulate, such as dioxins, concerns related to chronic effects can occur following an acute exposure. This concern results when a compound has low acute toxicity but is known to persist for long periods of time within the body. Following an acute exposure to such chemicals, the absorbed dose may be stored within in the body, and only slowly released into the blood stream. The consequence of this response to an acute event is a low-level release that effectively acts like a long-term dose

The primary concern with dioxin toxicity is chronic (*i.e.*, long-term) exposure. Typically, long-term low-level dioxin exposure occurs through consumption of contaminated food or from environmental sources. Such exposures can result in a number of well described adverse human health outcomes. The type of exposure that occurred during the 1966-67 herbicide trials at CFB Gagetown were quite different and may well have different outcomes. The short-term events that occurred during the trials may have resulted in elevated dioxin body burdens that would have peaked within a short time of exposure, and would have declined steadily since then. Estimated dioxin body burdens over time were calculated and compared with those indicative of adverse health effects.

The body burden approach is an accepted and well documented approach and has been utilized for the evaluation of chronic dioxin related risks following acute duration exposures (U.S. EPA, 2003; WHO, 2000a). For the evaluation of chronic exposures/chronic risks, and acute exposures/acute risks conventional risk assessment methods (HQ estimates) have been utilized.

The utility of the body burden approach for HCB is less certain and as such the evaluation of HCB related risks has followed more conventional risk assessment approaches. For chronic exposures/chronic risks, HQ and ILCR estimates have been provided for HCB, assuming annualized exposures over a maximum three year period (the trainee was assumed to return to the based for training over a three year period). For acute exposures/acute risks, HQ estimates have also been provided, these utilizing the acute duration TRV established by ATSDR (2002). The evaluation of cancer risks following acute duration exposures is an area of high uncertainty. ILCR estimates have been provided by multiplying the cancer slope factor with acute exposure estimates. Although of questionable relevance, this evaluation has been included due to the evidence that HCB remains in the body for an extended duration following short-term exposures. For the purpose of this evaluation, a duration of exposure of one year has been assumed even though these exposures occurred over a 3 or 4 day time span.

3.4.3 Consideration of Chemical Mixtures

Concurrent exposures to more than one chemical may result in interactions among toxicological effects; this may result in a combined toxicity which is equal to the sum of toxicities of the individual chemicals (additivity or independence), greater than the sum (synergism or potentiation) or less than the sum (antagonism). In general, toxicological interactions depend on the chemicals present, the levels of exposure to each, their mode of action and their concentrations. The likelihood of a biologically significant interaction occurring is a function of at least the physical, chemical and biological properties of the chemicals involved, their modes of action, and their concentrations. Most non-additive interactions can only be demonstrated at relatively high exposures, where clear adverse effects are observed. Such interactions have not been observed or quantified at the relatively low rates of exposure typical of those associated

with most environmental or occupational situations (NAS, 1983; Krewski and Thomas, 1992), and are therefore not typically considered in risk assessments. Additivity is generally recognized as the most plausible type of interaction that may occur in situations of chemical exposure in the ambient environment. However, it requires that the chemicals act through the same or similar mechanisms of action and/or affect the same target tissue(s). In HHRA's where the COCs act *via* different mechanisms of toxic action, and affect different target tissues, it is typically assumed that no potential toxicological interactions warrant consideration, and the estimated exposures and risks for the COCs are considered separately. Because PCDD and HCB act *via* unique mechanisms action and/or affect the same target tissue(s) the individual substances were evaluated separately.

4.0 PROBLEM FORMULATION

4.1 Chemicals of Concern (COCs)

For the Tier I risk assessment of the 1966-67 U.S. trials, the chemicals of concern are the manufacturing impurities (contaminants) of the herbicides applied during these trials. These contaminants include PCDD/PCDF and HCB.

The exposure point concentration (EPC) can be defined as the concentration of a COC in a specific environmental medium with which a receptor is expected to come into regular contact. Proper characterization of the EPC is critical to any traditional quantitative exposure assessment.

A retrospective assessment of human exposure to various herbicide contaminants (*i.e.,* dioxin) has been requested; however, historical EPC in various environmental media for these compounds was not available. EPC data must, therefore be developed using records of historical herbicide application events. Given the period of time under investigation (*i.e.,* 1966-67) and the persistent nature of some COCs, the development of time-dependent EPC data for all environmental media required historical spray application data and environmental fate and transport modeling.

Depending on the extent of data and historical records available, the reconstruction of historical exposures ranged from a qualitative discussion of potential exposures of individuals (based upon reviews of detailed quantitative studies conducted elsewhere) to a detailed quantitative assessment of historical exposure estimates based on detailed herbicide application data. EPCs are further characterized in Section 5.0.

4.2 Potential Receptors

Because the quantitative risk assessment does not look at all individuals on a case-by-case basis, it was important that a series of receptor groups be identified which can be used to represent all types of both civilian and military individuals. How and where these receptor groups will encounter the COCs while spending time both on and off the military base must be understood.

The following is a list of receptor groups, including a description of how these receptor groups might have encountered the COCs, that have been considered in this assessment:

- Mixer/Loader – These individuals were responsible for handling, mixing and loading the various herbicide products. It is assumed that these receptors could have come into direct contact with the COCs contained within the herbicide products during the handling, mixing and/or loading events. While it is possible that this task was divided amongst several individuals or teams, and that no one single person would have handled all of the applied herbicide during the numerous trials, the absence of historical data to validate this assumption required the use of this conservative approach. Total exposure to this receptor will be the sum of the individual exposures experienced during each of these activities. For the 1966-67 scenario, this group only included military personnel and it was assumed that different individuals were involved in each year. Exposures of the mixer/loader was assumed to occur during routine mixing and loading activities through the inhalation of vapours and dermal absorption through skin. An accidental scenario

was also evaluated in which the mixer/loader experiences an additional dermal exposure event as a result of a spill of concentrated herbicide.

- Applicator – These individuals are the pilots responsible for applying the herbicide products. For the 1966-67 scenario, this group only included military personnel. It was assumed that all herbicide active ingredients were in liquid form and that exposure occurred as a result of absorption through both dermal and inhalation routes.

- Flagger – The 1966 and 1967 aerial spray campaigns involved a number of individuals on the ground whose job was to assist the aerial applicator by marking specific locations to begin and end specific spraying events. A flagger was the individual that was responsible for marking the beginning or end of a plot targeted for the aerial application of herbicides. It was assumed that these receptors would be exposed to herbicide spray during each application event. It was also assumed that military personnel would be responsible for this activity and that an individual was involved in the flagging of all plots receiving chemical mixtures during either the 1966 or 1967 trials. Exposure occurred as a result of absorption through both dermal and inhalation routes. An accident scenario was also developed for the flagger which assumed that an individual would be directly sprayed with herbicide product.

- Post-Application Scouting – These individuals were responsible for entering the forested area sometime following the application of herbicides for the purpose of making field observations. It was assumed that these receptors would come into direct dermal contact with recently sprayed vegetation. It was assumed that military personnel would be responsible for this activity.

- On-Site Military Trainee – These military personnel were those who may have spent significant amounts of time in various areas of the base while completing military training, including survival training. It was assumed that this receptor group would have come into direct contact with various environmental media (*i.e*., soil, and wild berries) which have been contaminated by the COCs contained within the applied herbicide products. For the 1966-67 scenarios, it was assumed that training exercises occurred in direct proximity to the spray areas, during the time of the spraying. Potential direct spray exposures may have been similar to those experienced by the flagger and, therefore, was also considered as part of an accidental spray scenario.

Several receptor groups have not been included in the current assessment (Tier 1). These will be considered in subsequent Tiers. These include:

- Off-Site Civilian – These individuals are those who may have lived near the military base and occasionally used specific areas of the base for recreational purposes (*e.g*., hunting, walking, berry picking, *etc*.). It was assumed that this receptor group may have come into direct contact with various environmental media (*e.g*., soil, dust, local produce, *etc*.) which have been contaminated by the COCs contained within the applied herbicide products while living at home (*i.e.,* spray drift depositing on nearby off-site residential properties) and while spending time on the military base itself. This receptor group was not considered for the 1966-67 scenarios as these spray areas are fairly small and remote resulting in limited opportunities for exposures. REMSpC (2006) have estimated that

virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, indicating that off-site drift would not have occurred. It is noted that the former town of Inniskillen is greater than 10.2 km from both the 1966 and 1967 spray areas. The nearest off-site location to the 1966 spray area is approximately 3 km from the closest test plot. The 1966-67 spray areas will be considered as part of the evaluation of this receptor group during Tiers 2 and 3 exposure scenarios.

- Civilian Spouses – spouses of military personal may have come into contact with the COCs through contact with clothing brought home by military personnel following spray activities. These potential receptors were not considered as their exposures would have been small as compared to the military personnel directly involved in the spray activities, and as such, these concerns would be less than those quantitatively evaluated.

4.3 Exposure Pathways

Developing realistic exposure scenarios requires detailed information regarding who, what, where, when and how particular groups of individuals might have come into contact with the COCs present in the applied herbicide products. Figure 4-1 provides an overall conceptual framework, which outlines the general sources of exposures, the individuals of concern and the various ways in which these receptor groups might have encountered the COCs. From this, more detailed exposure scenarios were developed.

Several potential exposure pathways were eliminated from further consideration. These included:

- Groundwater – Task 2E has indicated that no potable groundwater wells exist in close proximity to the 1966 and 1967 spray areas (JW, 2006b). Base bivouac wells were installed in the mid-1990's and as such are not relevant to the current assessment. The Blissville well dates back to the 1960s; however, the well is more than 4 km from the closest trial plot. The very low solubility of PCDD and HCB (0.2 and 6 µg/L, respectively) and high log K_{ow} values (6.8 and 5.73, respectively) associated with the COCs preclude the likelihood that either PCDD or HCB would migrate from the spray areas to any potable water well either on the base or its immediate proximity. As such, this pathway was excluded from further consideration in Tier 1. These pathways will be considered for subsequent Tiers.
- Surface Water – No significant surface water receptors (those with known recreational uses such as fishing) were identified in the vicinity of the 1966 spray area (JW, 2006b). The 1967 spray area does lie within the watershed that drains the Nerepis River; however, the area is approximately 5 km from the main channel of the river (JW, 2006b). In addition, the very low solubility and high log K_{ow} values associated with the COCs preclude the likelihood that either PCDD or HCB would migrate from the spray areas to any surface water bodies either on the base or in its immediate proximity. As such, this pathway was excluded from further consideration in Tier 1. These pathways will be considered for subsequent Tiers.

- Hunting/fishing - this potential pathway was not considered for the 1966-67 scenario as these spray areas are fairly small and remote resulting in limited opportunities for exposures. REMSpC (2006) have estimated that virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, indicating that off-site drift would not have occurred. The 1966-67 spray areas will be considered as part of the evaluation of this pathway during Tiers 2 and 3 exposure scenarios.
- Brush clearing and burning - Brush clearing was not conducted manually in either 1966 or 1967. As such, pathways related to brush clearing and burning were not considered as part of the Tier 1 assessment. These pathways will be considered for subsequent Tiers.
- Volatilization following application – given the low vapour pressures of the COCs this pathway was not considered relevant.
- Contact with COCs in non-designated spray areas – based on the information provided by REMSpC (2006) which indicates that virtually all of the herbicide product would have deposited on the foliage and/or ground within 500 ft (152 m) of the flight line, drift to non-designated spray areas was not considered. Areas immediately adjacent to the spray plots were considered as part of the actual spray plots.

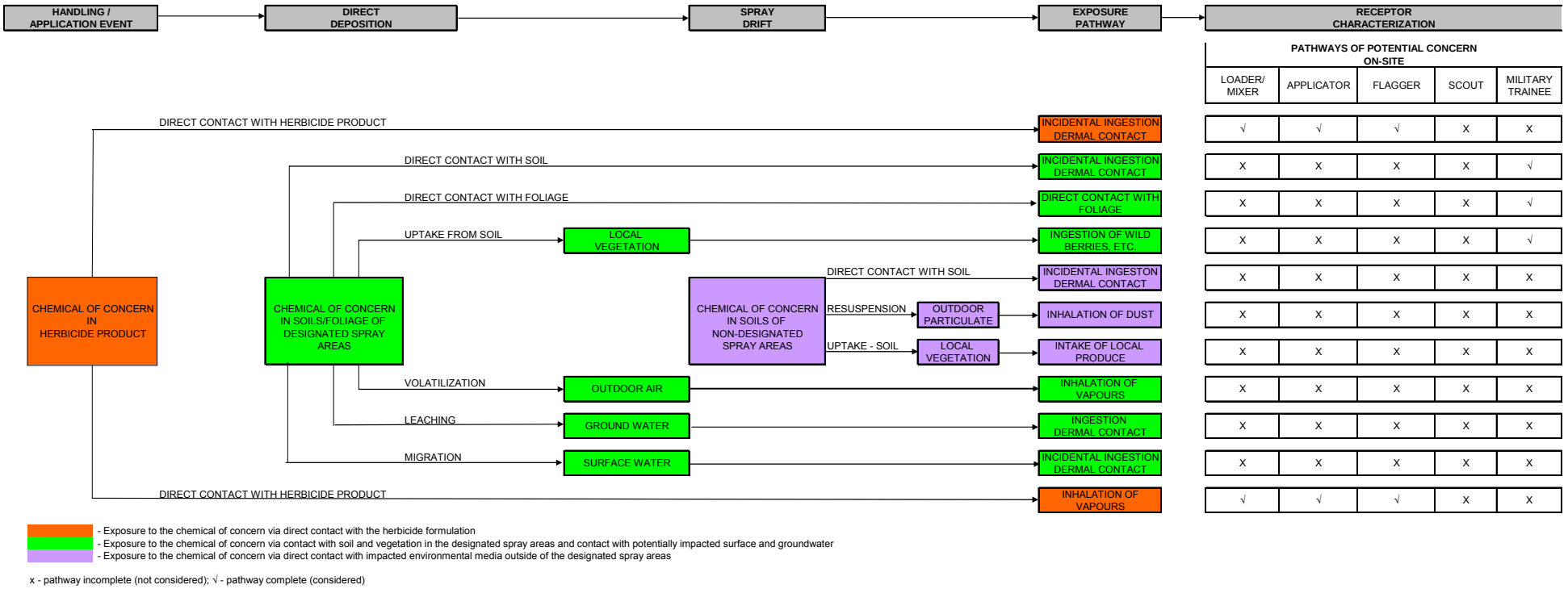
The spatial and temporal extent of environmental media impacted by historical spraying practices and the accessibility of these media to humans are of particular importance to the exposure assessment.

Exposures of individuals may be classified into two types of exposure, direct and indirect exposure. Direct exposure would result when an individual is within the general vicinity of the application area during a spraying event as illustrated in Figure 4-2.

Indirect exposures might occur as a result of an individual coming into contact with various environmental media that have been impacted by previous spraying events. Defining on- and off-site areas which may have been either directly affected by historical spray events and/or as a result of spray drift is a critical input to the historical reconstruction of exposure.

Given the period in which the historical reconstruction of exposure is to encompass (*i.e.,* 1966-67) and the persistent nature of some of the COC (*e.g.,* dioxin), it was necessary to conduct an aggregate exposure assessment, whereby the cumulative influences of successive plot spraying events would be considered.

Figure 4-1 Human Health Conceptual Model – Tier 1



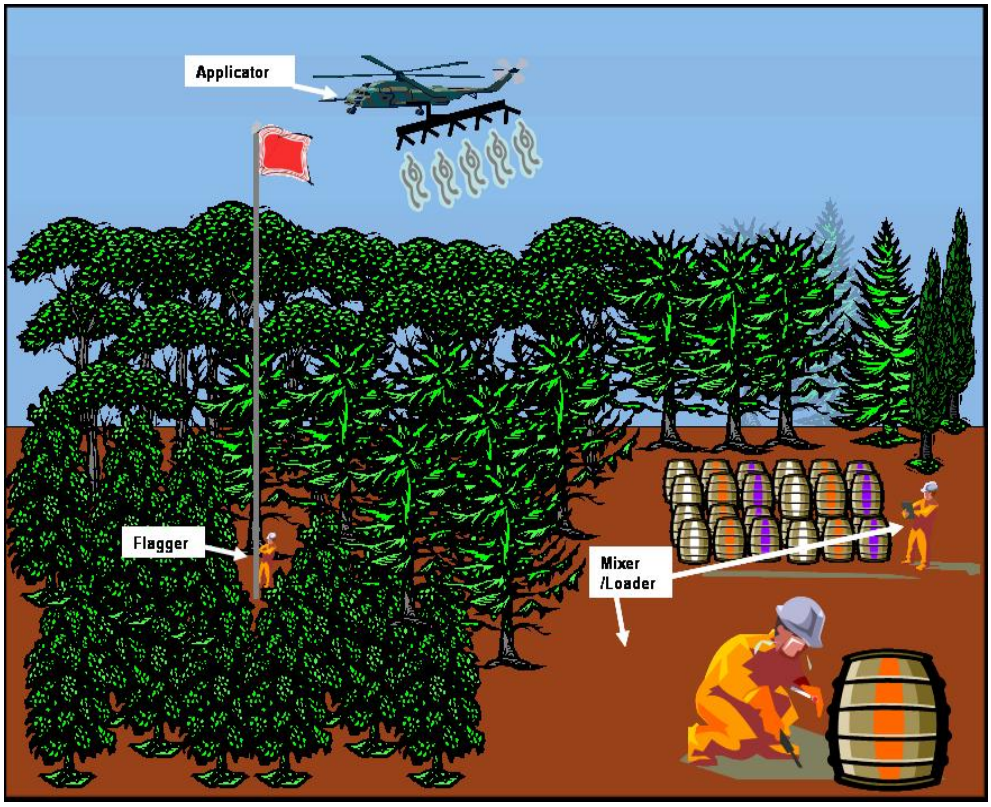


Figure 4-2 Conceptual Model of an On-site Rotary Wing Applicator and Military Personnel

4.3.1 Development of Exposure Scenarios

Developing exposure scenarios requires careful consideration of a number of exposure assumptions including the pathways through which exposure will occur, the physical and behavioural traits of the receptors, duration of exposure periods, and the influence of clothing or equipment on predicted exposure. Some of these issues are addressed for the receptors and activities previously described in Section 4.2. Exposure scenarios have been developed for the following receptor and exposure situations:

- Mixer/loader – routine
- Applicator – routine
- Flagger – routine
- Post Application Scout – routine
- Military Trainee – routine
- Mixer/loader – accident (spill)
- Flagger/trainee – accident (direct spray)

Further details related to the quantitative exposure assessment are provided in Section 5.0.

4.3.1.1 Mixer/Loader and Applicator

Receptors that are responsible for combining components of the herbicide mixture will be subject to exposure events that are unique to this activity. The same can be said for receptors involved in the loading of the herbicide mixture into application vessels as well as those involved in applying the herbicide to the targeted area. Estimating exposure to COCs during these events employed the use of exposure data provided by the Pest Management Regulatory Agency (PMRA), literature-based values, as well as a number of additional assumptions.

Dermal and inhalation exposure data for the mixer/loader and applicator scenarios can be estimated using predicted loading values from the Pesticide Handlers Exposure Database (PHED). PHED model runs for various scenarios were provided by PMRA. PHED provides generic passive dosimetry data for mixer/loader and applicator exposure scenarios specific to the formulation type, mixing and loading systems, application equipment, and level of personal protective equipment (PPE). To estimate exposure for each use scenario, appropriate subsets were created from the mixer/loader and applicator database files of PHED. Further details on PHED are provided in Appendix D.

All data were normalized for the amount (lbs or kilograms) of active ingredient handled based on the recorded application for each plot (total usually prepared for duplicate applications). Exposure estimates were prepared on the basis of the best-fit measure of central tendency, *i.e.*, summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part.

Personal Protective Equipment

Predicting dermal exposure during mixing, loading and application is highly dependent on the level of PPE worn during these activities. PHED data is available for dermal loading based on receptors using the following PPE:

a) Short pants, short sleeves and no gloves;
b) Long pants, short sleeves and no gloves;
c) Long pants, long sleeves and no gloves;
d) Single layer clothing with no gloves;
e) Single layer clothing with gloves;
f) Coveralls over single layer clothing with gloves; and,
g) Chemical resistant coveralls with gloves.

Coveralls are assumed to provide a 75% protection factor for arms, chest, back, thigh and lower legs. Chemical resistant coveralls are assumed to provide a 90% protection factor for arms, chest, back, thigh and lower legs.

Failure to identify documentation to indicate if appropriate PPE was used during the mixing, loading and application of COCs. As a result, conservative assumptions are made to ensure that potential exposures are not underestimated. This may include the use of dermal loading data for clothing scenarios a to c as listed above which are more representative of individuals wearing casual clothing rather than clothing typically worn for handling herbicides.

Formulation Type

Predicting exposures during the mixing and loading stages is dependent on the herbicide formulation type. PHED data is provided for the following formulation types:

a) Dry flowable;
b) Granular;
c) All liquids; and,
d) Wettable powder.

Based on available documentation, it is anticipated that all components of the applied herbicide mixtures were in liquid phases at the time of mixing.

Mixing and Loading Systems

Systems used for mixing and loading chemicals are generally defined as either Open or Closed. As to be expected, open mixing and loading systems result in significantly higher rates of exposure than closed systems. As described for PPE, failure to identify documentation to indicate that the systems used were closed may require that conservative assumptions be applied and that dermal loading and inhalation exposures be based on data developed for open systems.

Application Equipment

Based on review of historical documentation, the application of herbicides was through aerial methods. PHED data are available to describe dermal loading and inhalation exposure to an applicator within a fixed-wing and rotary wing plane. It is understood that herbicides were applied using a helicopter in the 1966-67 trials and using various planes for the remaining application periods. Failure to identify exposure details specific to helicopter applications may necessitate the use of this data for all applicator scenarios.

4.3.1.2 Flagger/Post-Application Scout

Application of herbicides through aerial methods may involve individuals on the ground marking or flagging the location at which the applicator should begin and/or end spraying. These receptors may be subject to exposure through various pathways including inhalation of fine mists and dermal contact. As described for the mixer/loader and applicator scenarios, the use of PPE will have a significant effect on the degree of exposure during these events. PHED data describing inhalation and dermal exposure is available for a typical flagger exposure scenario for a number of assumptions of PPE use.

Following application it was necessary to assess the effectiveness of each combination of herbicide applied and the concentration-response noted for each plot in the trials. As a result, post-application scouting activities were assumed to occur immediately following application to assess the penetration of the herbicide through the upper canopy. The post-application scout was conservatively assumed to come into direct dermal contact with recently sprayed vegetation as he makes his way through each test plot.

4.3.1.3 On-Site Military Trainee

Historical records indicate that areas affected by herbicide applications may have been used as grounds for training military personnel. These receptors may have spent extended periods of time living within these areas and consuming food items (*i.e.*, wild berries) from the local environment. The two main areas of uncertainty associated with predicting exposure through this pathway include the amount of wild berries consumed as well as the concentration of COCs in the wild berries. Exposure to COCs may have also occurred *via* dermal contact and incidental ingestion of impacted soil.

4.3.1.4 Flagger/Trainee – Accidental Spray Event

An additional exposure scenario, wherein a flagger and/or a military trainee was inadvertently sprayed during the application event, was also considered. This scenario was undertaken to evaluate the unlikely event that an individual may have been present within or adjacent to a spray zone during the time of herbicide application. This individual was assumed to receive a direct spray, at worst-case application and deposition rates, with no canopy cover protection. Accidental spray incidents are also accounted for in the PHED scenarios.

4.3.1.5 Civilians

Civilian receptors may occasionally visit military property for a number of purposes including hunting, fishing, berry collection or general recreation. As a result, receptors may be exposed to COCs *via* inhalation, incidental ingestion, and dermal contact of contaminated soil as well as through ingestion of fish, local game, or local wild berries.

Civilian receptors may also have been exposed to COCs as a result of herbicide spray drifting to areas outside of the military property line.

This receptor group was not considered for the 1966-67 scenario as these spray areas are fairly small and remote resulting in limited opportunities for exposures. The 1966-67 spray areas will be considered as part of the evaluation of this receptor group during Tier 2 and 3 exposure scenarios. Further details have previously been provided.

5.0 EXPOSURE ASSESSMENT

The primary objective of the exposure assessment is to predict, using a series of realistic albiet conservative assumptions, the rate of exposure of human receptors to PCDD and HCB through the exposure scenarios and pathways identified in the problem formulation phase.

5.1 Estimated Daily Intake (EDI) Values

All Canadians are exposed to low levels of dioxins and HCB through background or non-site related sources such as air, water, soil and foods including those purchased from supermarkets. EDI values are estimates of background exposures to the COCs which occur as a result of normal activities unrelated to herbicide use at CFB Gagetown.

5.1.1 Dioxins

Historical EDI rates for the Canadian population are difficult to estimate for years prior to the 1980s due to a paucity of data. Lorber (2002) has estimated that EDIs in the 1960s and 1970s were as high as 6.0 pg TEQ/kg bw/day. This value has been utilized to represent EDIs reflective of exposures in the 1960s and 1970s. Canadian data for PCDD and PDCFs concentrations in environmental media and food were utilized to determine EDI values for the 1980s and onward. The EDI value of 1.76 pg TEQ/kg bw/day was estimated to reflect exposures during the 1980s and early 1990s (Table 5-1). The EDI for a lifetime receptor in the present day was estimated as 0.905 pg TEQ/kg bw/day (Table 5-1). A detailed summary of the datasets and calculations used to establish the above mentioned estimated daily intake values are available in Appendix C-1.

Table 5-1 Canadian Estimated Daily Intake Rates for PCDD/PCDFs

Environmental Media	Estimated Daily Intake		
	1960s-1970s (pg TEQ/kg bw/day)	1980s-1995 (pg I-TEQ/kg bw/day)	1996 - present (pg TEQ-WHO_{98}/kg bw/day)
Soil	-	0.003	0.003
Air	-	0.010	0.010
Water	-	0.001	0.001
Consumer Products	-	0.011	0.011
Food	-	1.74	0.88
TOTAL	**6.0**	**1.76**	**0.905**

5.1.2 Hexachlorobenzene

Historical and current EDI values were characterized for HCB using Canadian data. The historical EDI value for a lifetime receptor employed for historical reconstruction was 6.2 ng/kg bw/day (Table 5-2). The current EDI for a lifetime receptor in is 0.16 ng/kg bw/day (Table 5-2). A detailed summary of the datasets and calculations used to establish the above mentioned estimated daily intake values are available in Appendix C-2.

Table 5-2 Canadian Estimated Daily Intake Rates for HCB (ng/kg bw/day)

Environmental Media	Estimated Daily Intake (ng/kg bw/day)	
	Historical	Current
	Lifetime Receptor	Lifetime Receptor
Soil	--	0.05
Air	--	0.002
Water	--	0.0005
Food	--	0.10
TOTAL	**6.2**	**0.16**

5.2 Characterization of Potential Receptors

For the current assessment, the exposure of five distinct receptor groups was quantitatively evaluated based on historical documentation of preparation and application practices. Where historical records did not provide sufficient detail to guide the exposure assessment, conservative assumptions based on methodologies used by reputable agencies such as PMRA, Health Canada, the U.S. Bureau of Land Management and the U.S. Department of Agriculture Forest Service were used to supplement the project-specific information.

One of the primary sources of exposure parameters was the Pesticide Handler Exposure Database (PHED). This is a database that contains voluntarily submitted empirical exposure data for workers involved in the handling or application of pesticides in the field (OPPT, 2006). It was developed by a task force which includes representatives from Health Canada, the U.S. EPA, and the National Agricultural Chemicals Association (Leighton and Nielsen, 1995). The database contains data for over 2000 monitored exposure events. PHED is a compilation of generic mixer/loader, flagger, and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. Exposure estimates are presented on the basis of the best-fit measure of central tendency, *i.e.*, summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part.

The basic assumption underlying the system is that exposure to pesticide handlers can be calculated generically, based on the available empirical data for chemicals, as worker exposure is primarily a function of the formulation type and the handling activities (*e.g.*, packaging type, mixing/loading/application method, and clothing scenario), rather than chemical-specific properties. The use of generic data that does not directly address chemical properties of a herbicide is most appropriate. The experience in agriculture and forestry applications is that the formulation, the method of application, the label rate of application, the percent active ingredient, and the number of acres treated, but not the chemical properties of the pesticide, control the amount of dermal and inhalation exposure. Thus, PHED allows exposure and risk assessments to be conducted with a much larger number of observations than would be available from a single exposure study, thus increasing the confidence in the assessment (U.S. EPA, 2000). Refer to Appendix D for a detailed description of the PHED approach.

As described in the problem formulation, the activities of five receptor groups (mixer/loader, applicator, flagger, field scout, and military trainee) make these individuals particularly susceptible to exposure to the contaminants in the applied herbicides. This is a result of their roles in the preparation and application of the herbicide mixtures, or their activities during time

spent within the areas receiving the applications. The details surrounding the predicted exposures for these receptors are provided in Section 5.3.

5.3 Exposure Characterization

Details regarding parameters used in the exposure assessment, including those for which a range of values have been used, as well as the application rates of PCDD and HCB, are provided in Sections 5.3.1 and 5.3.2, respectively. Appendix E contains a detailed 'worked example' for one herbicide plot, illustrating all input parameters and exposure/risk calculations.

5.3.1 High, Low and Central Tendency Exposure Estimates

The current exposure assessment has provided a range of potential exposures for each scenario. The range is described by three individual estimates of exposure, including a high, low and central estimate. The high-case estimate employs a series of individual worst-case assumptions, applied one after another, introducing a repetitive input parameter selection bias. The high-case estimates truly represent a worst-case scenario. Similarly, the central and low exposure estimates employed, whenever possible, central (average) and low-end exposure parameters, respectively. The parameters that vary across each of the three exposure estimates are discussed in Sections 5.3.1.1 to 5.3.1.3. Not all input parameters were associated with a range (*i.e.,* a low, central and high estimate). Some input parameters (*e.g.,* body weight, soil ingestion, *etc.*) were assigned a single value which was applied to each exposure estimate. A range of potential exposure values (facilitated through the use of selected low, central and high input parameters) were developed to provide a general appreciation for the level of uncertainty and variability present within the quantitative exposure estimates.

5.3.1.1 PCDD and HCB Content of Herbicide Mixtures

As previously discussed, and detailed in Appendix A, a review of the scientific literature indicated that the PCDD content in Agent Orange and 2,4,5-T was represented by an average concentration of 2 µg TCDD/g AO&2,4,5-T (ppm weight:weight) (range 0.02 to 15 µg/g). Data from the literature allowed for the use of a range to characterize the PCDD content in Agent Purple (AP) of 5 to 45 ug TCDD/g AP was employed with a central tendency value of 32.8 ug TCDD/g AP. Contaminant levels in PCP ranged from 2.2 to 45 ug TEQ/g PCP (central tendency value of 9.2 µg TEQ/g PCP). The HCB content in Picloram was determined to be 200 µg HCB/g Picloram (ppm weight:weight). Table 5-3 summarizes the contaminant content of Agent Orange, Purple, 2,4,5-T, pentachlorophenol and Picloram, expressed as a fraction.

Table 5-3 Contaminant Content Expressed µg/g of Active Ingredient

Contaminant	HCB	Dioxins (TEQ)		
		Low	Central	High
Agent Orange/2,4,5-T	-	0.02	2.0	15.0
Agent Purple	-	17.0	32.8	45.0
Pentachlorophenol (timbertox)		2.2	9.2	45.0
Picloram	200			

5.3.1.2 Dermal Absorption

Under a number of the exposure scenarios, receptors were assumed to come into direct contact with herbicide mixtures either during preparation of the mixtures or during application. Once the herbicide product makes contact with exposed skin, a method described by the Syracuse Research Corporation (SERA, 1997; 2001) was used to predict the proportion of the applied dermal dose that may be absorbed. As described by SERA (2001), dermal absorption rates (or k_a values expressed as amount per unit time or as reciprocal time) and dermal penetration rates (or k_p values expressed as cm/hour) are commonly required for dermal exposure scenarios.

According to SERA (2001), dermal absorption rates are used to estimate the absorbed dose associated with dermal deposition. Dermal absorption rates (k_a values) express the amount or proportion of chemical absorbed into the body per unit time. Based on work conducted by Durkin *et al.* (1995), SERA (2001) concluded that first-order dermal absorption rates (k_a values) rather than penetration rates (k_p) should be used when describing exposure scenarios involving the deposition of a chemical on to the skin surface. The use of k_p values is more applicable to describing scenario whereby the skin is immersed an aqueous solution. SERA (1997, 2001) determined that dermal first-order absorption rate coefficients were best described using both molecular weight and the logarithm of the octanol-water partitioning coefficient (K_{ow}) as follows:

Equation 3

$$Log_{10} k_{a(\,first\ order\,)} = 0.233\ Log_{10} Kow - 0.00566\ MW - 1.49$$

where:

k_a	=	Chemical-specific first-order absorption dermal rate coefficient (hr^{-1})
K_{ow}	=	Chemical-specific octanol-water partitioning coefficient (unitless)
MW	=	Chemical-specific molecular weight (g/mol)

The methods provided by SERA (2001) and USDA (2003) were used to derive first-order dermal absorption rates (and associated 95% confidence intervals) for PCDD and HCB. For PCDD, the physical/chemical data of the 2,3,7,8-TCDD congener was to derive k_a values. As indicated, first-order dermal rates constants are time dependent and, therefore, the amount of time a liquid is in contact with exposed skin must be provided. Based on the methods provided by SERA (2001), upper and lower confidence limits for dermal absorption rates (k_a) were derived. Central exposure estimates employed the most likely k_a value while the upper and lower exposure estimates used the upper and lower 97.5% confidence limits on the mean k_a values, respectively. Refer to Appendix E for the methods used to predict upper and lower 97.5 percent confidence limits for k_a.

The following equation provides the method used to derive the proportion of chemical absorbed per unit time.

Equation 4

$$P = 1 - e^{-k_a t}$$

where:

P = Proportion of PCDD or HCB absorbed through the skin in time t
k_a = Chemical-specific first-order absorption dermal rate coefficient (hr^{-1})
t = Amount of time in exposed skin is in contact with contaminant

5.3.1.3 Use of Personal Protective Equipment

Use of the PHED data for predicting exposure to the mixer/loader, applicator and flagger, allows for the use of exposure factors that are dependent on the level of PPE used during each activity. For the current assessment, the central tendency dermal exposure is based on a scenario in which the receptor is wearing a single layer of clothing with gloves. The low exposure estimate assumes the receptor is wearing coveralls over a single layer of clothing with gloves, and the high exposure estimate assumes the receptor is only wearing a single layer of clothing with no gloves. Refer to Appendix D for a detailed discussion of the PHED approach.

5.3.2 Application Rates

For each spray campaign (1966 and 1967) those plots which were sprayed with herbicide products containing the contaminants of interest (*i.e.,* PCDD and HCB) were identified. Contaminant application rates at each plot were calculated based on the formulation of the herbicide product, the application rate and the concentration of contaminant in each product.

Tables 5-4 through 5-6 provide the herbicide mixture, the application rate of the active ingredient, and the application rate of the contaminant (*i.e*., PCDD or HCB) for each of the plots evaluated in the current assessment. The contaminant application rates are a function of content of the contaminant within the given active ingredient. As described in Section 5.3.1.1, the estimated content of PCDD in Agent Purple has varied, and as a result, central, low, and high estimates were included in the assessment. Application rates provided in Tables 5-4 to 5-7 are expressed in units of g/m^2. For use in the exposure equations provided in Section 5.4, these rates are converted to lbs/acre by applying a conversion factor of 1 g/m^2 = 8.9 lbs/acre.

Table 5-4 Application Rates of Herbicide Mixtures and Dioxin TEQ in the 1966 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixture		TEQ Application Rate (g/m^2)		
		(g/m^2)	(lbs/acre)	Low	Central	High
1	Purple + diesel (1:1)	1.77	15.75	3.0E-05	5.8E-05	7.9E-05
2	Purple + diesel (1:1)	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
3	Purple + diesel (1:1)	0.59	5.25	1.0E-05	1.9E-05	2.6E-05
4	Purple + diesel (1:2)	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
5	Purple + diesel (1:1)	1.77	15.75	3.0E-05	5.8E-05	7.9E-05
6	Purple + diesel (1:1)	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
7	Purple + diesel (1:1)	0.59	5.25	1.0E-05	1.9E-05	2.6E-05
8	Purple + diesel (1:2)	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
9	Purple, no diluent	3.53	31.5	6.0E-05	1.2E-04	1.6E-04
10	Purple, no diluent	2.35	21	4.0E-05	7.7E-05	1.1E-04

Table 5-4 Application Rates of Herbicide Mixtures and Dioxin TEQ in the 1966 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixture		TEQ Application Rate (g/m^2)		
		(g/m^2)	(lbs/acre)	Low	Central	High
11	Orange, no diluent	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
12	Purple, no diluent	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
13	Orange, no diluent	2.35	21	4.7E-07	4.7E-06	3.5E-05
14	Purple, no diluent	3.53	31.5	6.0E-05	1.2E-04	1.6E-04
15	Orange, no diluent	3.53	31.5	7.1E-07	7.1E-06	5.3E-05
16	Purple, no diluent	2.35	21	4.0E-05	7.7E-05	1.1E-04
17	Orange, no diluent	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
18	Purple, no diluent	1.18	10.5	2.0E-05	3.9E-05	5.3E-05
19	Orange, no diluent	2.35	21	4.7E-07	4.7E-06	3.5E-05
20	70% D + 30%T + diesel (1:1)	1.77	15.75	3.5E-07	3.5E-06	2.6E-05
21	Orange, no diluent	3.53	31.5	7.1E-07	7.1E-06	5.3E-05
22	70% D + 30%T + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
23	Orange + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
24	70% + 30%T + diesel (1:1)	0.59	5.25	1.2E-07	1.2E-06	8.8E-06
25	Orange + diesel (1:1)	0.59	5.25	1.2E-07	1.2E-06	8.8E-06
26	70%D + 30%T + diesel (1:1)	1.77	15.75	3.5E-07	3.5E-06	2.6E-05
27	70%D + 30%T + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
28	Orange + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
29	Orange + diesel (1:1)	1.77	15.75	3.5E-07	3.5E-06	2.6E-05
30	70%D + 30%T + diesel (1:1)	0.59	5.25	1.2E-07	1.2E-06	8.8E-06
31	Orange + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
32	70%D + 30%T + diesel (1:1)	3.53	31.5	7.1E-07	7.1E-06	5.3E-05
33	Orange + diesel (1:1)	0.59	5.25	1.2E-07	1.2E-06	8.8E-06
34	**NOT SPRAYED**	0.00	0	0.0E+00	0.0E+00	0.0E+00
35	Orange + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
36	70%D + 30%T + diesel (1:1)	2.35	21	4.7E-07	4.7E-06	3.5E-05
37	Orange + diesel (1:1)	1.77	15.75	3.5E-07	3.5E-06	2.6E-05
38	70%D + 30%T + diesel (1:1)	1.18	10.5	2.4E-07	2.4E-06	1.8E-05
39	70%D + 30%T + diesel (1:1)	3.53	31.5	7.1E-07	7.1E-06	5.3E-05
46	M-2993 + diesel (1:1)	0.45	5	9.0E-08	9.0E-07	6.7E-06
48	M-2993 + diesel (1:1)	0.22	2.5	4.5E-08	4.5E-07	3.4E-06
50	M-2993 + diesel (1:1)	0.45	5	9.0E-08	9.0E-07	6.7E-06
52	M-2993 + diesel (1:1)	0.22	2.5	4.5E-08	4.5E-07	3.4E-06
58	M-2993 + diesel (1:2)	0.30	3.32	6.0E-08	6.0E-07	4.5E-06
62	M-2993 + diesel (1:2)	0.30	3.32	6.0E-08	6.0E-07	4.5E-06

Table 5-5 Application Rates of Herbicide Mixtures and HCB in the 1966 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixtures		HCB Application Rate (g/m^2)
		(g/m^2)	(lbs/acre)	
46	M-2993 + diesel (1:1)	0.11	5	2.2E-05
48	M-2993 + diesel (1:1)	0.06	2.5	1.1E-05
50	M-2993 + diesel (1:1)	0.11	5	2.2E-05
52	M-2993 + diesel (1:1)	0.06	2.5	1.1E-05
58	M-2993 + diesel (1:2)	0.07	3.32	1.5E-05
62	M-2993 + diesel (1:2)	0.07	3.32	1.5E-05
60	Phytar 160 + Tordon 22K (3:1)	0.06	0.5	1.1E-05
64	Phytar 160 + Tordon 22K (3:1)	0.06	0.5	1.1E-05
66	Diquat + Tordon 22K (1:1)	0.22	2.0	4.5E-05
68	Diquat + Tordon 22K (1:1)	0.11	1.0	2.2E-05
70	Diquat + Tordon 22K	0.22	2.0	4.5E-05
72	Diquat + Tordon 22K (1:1)	0.11	1.0	2.2E-05
74	Diquat + Tordon 101 (1:1)	0.06	0.5	1.1E-05
76	Diquat + Tordon 101 (1:1)	0.03	0.3	5.6E-06
78	Diquat + Tordon 101 (1:1)	0.06	0.5	1.1E-05
80	Diquat + Tordon 101 (1:1)	0.03	0.3	5.6E-06
82	Phytar 160 + Tordon 101 (1:1)	0.06	0.5	1.1E-05
84	Phytar 160 + Tordon 101 (1:1)	0.03	0.3	5.6E-06
86	Phytar 160 + Tordon 101 (1:1)	0.06	0.5	1.1E-05
88	Phytar 160 + Tordon 101 (1:1)	0.03	0.3	5.6E-06
90	Tordon 22K + Water (1:1)	0.34	3.0	6.7E-05
92	Tordon 22K + Water (1:1)	0.22	2.0	4.5E-05
94	Tordon 22K + Water (1:1)	0.11	1.0	2.2E-05
96	Tordon 22K + Water (1:1)	0.34	3.0	6.7E-05
98	Tordon 22K + Water (1:1)	0.22	2.0	4.5E-05
100	Tordon 22K + Water (1:1)	0.11	1.0	2.2E-05

Table 5-6 Application Rates of Herbicide Mixtures and TEQ in 1967 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixtures		TEQ Application Rate (g/m^2)		
		(g/m^2)	(lbs/acre)			
17	Orange	2.91	26	5.8E-06	5.8E-07	4.4E-05
18	Orange	2.91	26	5.8E-06	5.8E-07	4.4E-05
2	Penta/Timbertox	1.35	12	1.2E-05	3.0E-06	6.1E-05
49	Penta/Timbertox	1.35	12	1.2E-05	3.0E-06	6.1E-05
3	HCA + 2,4,5-T	0.67	6	1.3E-06	1.3E-07	1.0E-05
48	HCA + 2,4,5-T	0.67	6	1.3E-06	1.3E-07	1.0E-05
33	Orange	2.91	26	5.8E-06	5.8E-07	4.4E-05

Table 5-7 Application Rates of Herbicide Mixtures and HCB in the 1967 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixtures		HCB Application Rate (g/m^2)
		(g/m^2)	(lbs/acre)	
7	Paraquat +Tordon 22K	0.22	2.0	4.5E-05
8	Paraquat +Tordon 22K	0.34	3.0	6.7E-05
10	Diquat + Tordon 22K	0.22	2.0	4.5E-05
11	Diquat + Tordon 22K	0.22	2.0	4.5E-05
12	Picloram ester/M3142	0.67	6.0	1.3E-04

Table 5-7 Application Rates of Herbicide Mixtures and HCB in the 1967 Trials

Plot #	Herbicide Mixture	Application Rate of Herbicide Mixtures		HCB Application Rate (g/m^2)
		(g/m^2)	(lbs/acre)	
13	Picloram -Dalapon/M3189	0.50	4.5	1.0E-04
14	Tordon 22K/Picloram	0.34	3.0	6.7E-05
15	Tordon 22K/Picloram	0.50	4.5	1.0E-04
16	Tordon 101/White	0.18	1.6	3.6E-05
44	Paraquat +Tordon 22K	0.22	2.0	4.5E-05
43	Paraquat +Tordon 22K	0.34	3.0	6.7E-05
41	Diquat + Tordon 22K	0.22	2.0	4.5E-05
40	Diquat + Tordon 22K	0.22	2.0	4.5E-05
39	Picloram ester/M3142	0.67	6.0	1.3E-04
38	Picloram -Dalapon/M3189	0.50	4.5	1.0E-04
37	Tordon 22K/Picloram	0.34	3.0	6.7E-05
36	Tordon 22K/Picloram	0.50	4.5	1.0E-04
35	Tordon 101/White	0.18	1.6	3.6E-05

5.4 Detailed Exposure Methods

The general methods used to calculate exposure to receptors within each of the five receptor groups are provided in Sections 5.4.1 to 5.4.5. Refer to Appendix E for a detailed 'Worked Example' of the exposure and risk calculations.

Several different approaches are available when attempting to quantify exposures of individuals to COCs. The PHED approach is one of a number of approaches considered in the current exposure assessment. ENSR (2005) has conducted an extensive risk assessment for the Nevada Bureau of Land Management. The U.S Forestry Service (USDA, 2003) has also conducted similar risk assessments. Both assessments have employed the use of routine and accidental/incidental exposure scenarios. The alternate method for the Flagger was based on both the ENSR (2005) approach and the dermal absorption methods provided by SERA (2001) and USDA (2003). ENSR (2005) developed a Direct Spray scenario whereby a receptor is accidentally sprayed directly with a herbicide product because the receptor has entered the spray area during operations. Unlike the PHED approach, which relies on a database of historical measured data, the alternative approach uses traditional risk assessment exposure approximation techniques. Refer to Appendix E for the detailed equations and input parameters.

Although it has been suggested that the PHED approach accounts for accidental spills, it was considered appropriate, as per ENSR (2005) to provide traditional quantitative exposure estimates of these types of accidental exposures. It is unclear to CEI, based on the PHED data provided how the application practices of the last 10 to 20 years compares with the activities of the 1966 and 1967 trials. Secondly, it is unclear how the accident data included in the PHED values have been incorporated into the final UE values. Although these data inherently includes the frequency and magnitude of accidental exposures over a prolonged period of time, the exposure event of concern occurred over a one day period and, therefore, may not be comparable to the long-term exposure duration of a pesticide applicator.

5.4.1 Mixer/Loader

The exposure assessment assumed that an individual was involved in mixing and loading all of the herbicide solutions applied during the 1966-67 trials. While it is possible that this task was divided amongst several individuals or teams, and that no one single person would have handled all of the applied herbicide during the numerous trials, the absence of historical data to validate this assumption required the use of this conservative approach.

Exposures of the mixer/loader to PCDD and HCB was assumed to occur during routine mixing and loading activities through the inhalation of vapours and dermal absorption through skin. An accidental scenario was also evaluated in which the mixer/loader experiences an additional dermal exposure event as a result of a spill of concentrated herbicide. Exposures as a result of both the routine and accidental exposure scenarios are described below.

5.4.1.1 Exposure Resulting from Routine Mixing and Loading

This scenario involved predicting inhalation and dermal exposure experienced by the mixer/loader during routine activities. PHED provides generic passive dosimetry data for generic mixer/loader/applicator exposure scenarios specific to the formulation type, mixing and loading systems, application equipment, and level of personal protective equipment (PPE). PHED unit exposure values (UEs) were used to predict exposures under this scenario. It was assumed that all herbicide active ingredients were in liquid form and that mixing and loading was done with open systems. The PHED dermal UEs, which are an expression of the amount of chemical dermally deposited onto the receptor based on the amount of chemical handled, are dependent on the use of PPE. The inhalation UEs are divided into light and moderate exposures (Table 5-7).

When using the PHED approach to predict exposures of individuals to herbicide mixtures, body weight (70.7 kg as per Health Canada, 2004a) was the only receptor-specific input parameter required. In other words, the PHED approach expresses dermal exposure (for routine activities) as a function of application rate, area treated, dermal units (refer to Table 5-8) and the proportion of applied dose absorbed through the skin. A body weight of 70.7kg remained constant for all exposure levels (*i.e.,* low, central and, high).

Table 5-8 PHED Unit Exposure Values for the Mixer/Loader for Low, Central, and High Exposure Estimates (mg/lb chemical handled)

Exposure Level	Dermal Exposure				Inhalation Exposure
	Clothing Scenario	Body Exposure	Hand Exposure	Total Dermal Exposure	
Low	Coveralls over single layer with gloves	8.2E-03	6.72E-03	1.49E-02	7.26E-04
Central	Single layer with gloves	1.65E-02	6.72E-03	2.32E-02	1.13E-03
High	Single layer without gloves	1.65E-02	2.84E+00	2.86E+00	

Using the PHED UEs presented in Table 5-8, and the application rates presented in Tables 5-4 to 5-7, the dermal and inhalation exposures were calculated as follows:

Equation 5

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

where:

$EXP_{Dermal\ Routine}$	=	Dermal exposure from routine activities (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Area Treated (acres/day)
UE_{Dermal}	=	Dermal Unit exposure (mg/lb chemical handled)
P	=	proportion of applied dermal dose absorbed (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

and

Equation 6

$$EXP_{Inhal\ Routine} = \frac{AR \times AT \times UE_{Inhal} \times CF \times IAF}{BW}$$

where:

$EXP_{Inhal\ Routine}$	=	Inhalation exposure from routine activities (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Acres Treated per day (acres/day)
UE_{Inhal}	=	Inhalation Unit exposure (mg/lb chemical handled)
IAF	=	Inhalation Absorption Factor (chemical specific) (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

5.4.1.2 Exposure Resulting from an Accidental Spill

In addition to the routine dermal exposure experienced by the mixer/loader during the preparation of the herbicide mixtures, it is assumed that this receptor will receive a direct spill of the concentrated herbicide prior to mixing. This is assumed to occur once per day and to involve the herbicide mixture with the highest concentration of PCDD or HCB. Exposure is only assumed to occur through dermal absorption. This exposure is calculated as follows:

Equation 7

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

where:

$EXP_{Accidental}$	=	Predicted exposure through accidental dermal contact (ng/kg bw/day)
S	=	Spill amount (0.5 L/day of herbicide mixture; ENSR, 2005)
AC	=	Concentration of PCDD or HCB in herbicide mixture (g/L)
CF	=	Conversion Factor (1000 mg/g)
SAR	=	Surface Area Ratio (0.44; ENSR, 2005)
P	=	proportion of applied dermal dose absorbed (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body weight (kg)

The surface area ratio (SAR) is the ratio of the exposed surface area to the total body surface area. It assumes that 80% of the spill amount is to the clothing with a 30% penetration rate, and 20% is spilled to exposed skin ((0.8*0.3)+ 0.2= 0.44)) (ENSR, 2005).

5.4.2 Applicator

Exposure estimates for a chemical applicator were based on PHED UEs for aerial fixed-wing and rotary-wing liquid application. It was assumed that a single applicator was responsible for the application of all chemical mixtures during the 1966 and 1967 trials and that all herbicide active ingredients were in liquid form. Exposure occurred as a result of absorption through both dermal and inhalation routes. As described previously, UEs for three levels of PPE were included in the assessment (Table 5-9). When using the PHED approach to predict exposures of individuals to herbicide mixtures, body weight (70.7 kg as per Health Canada, 2004a) was the only receptor-specific input parameter required. In other words, the PHED approach expresses dermal exposure (for routine activities) as a function of application rate, area treated, dermal units (refer to Table 5-9) and the proportion of applied dose absorbed through the skin. A body weight of 70.7kg remained constant for all exposure levels (*i.e.,* low, central and, high).

Table 5-9 PHED Unit Exposure Values for the Applicator for Low, Central, and High Exposure Estimates (mg/lb chemical handled)

Exposure Level	Dermal Exposure				Inhalation Exposure
	Clothing Scenario	Body Exposure	Hand Exposure	Total Dermal Exposure	
Low	Coveralls over single layer with gloves	7.0E-04	2.5E-03	3.2E-03	3.2E-05
Central	Single layer with gloves	2.4E-03	2.5E-03	4.8E+00	4.9E-05
High	Single layer without gloves	2.4E-03	2.0E-03*	4.4E-03	

* The dermal exposure to the hands without gloves is lower than that for hands with gloves. The PHED data indicates that there is high confidence in the single layer without gloves scenario.

Using the PHED UEs presented in Table 5-9, and the application rates presented in Tables 5-4 to 5-7, the dermal and inhalation exposures were calculated as follows:

Equation 8

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

where:

EXP_{Dermal}	=	Dermal exposure (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Acres Treated per day (acres/day)
UE_{Dermal}	=	Dermal Unit exposure (mg/lb chemical handled)
P	=	Proportion of applied dermal dose absorbed (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

and

Equation 9

$$EXP_{Inhal} = \frac{AR \times AT \times UE_{Inhal} \times CF \times IAF}{BW}$$

where:

EXP_{Inhal}	=	Inhalation exposure (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Acres Treated per day (acres/day)
UE_{Inhal}	=	Inhalation Unit exposure (mg/lb chemical handled)
IAF	=	Inhalation Absorption Factor (chemical specific) (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

5.4.3 Flagger

The 1966 and 1967 aerial spray campaigns involved a number of individuals on the ground (*i.e.*, flaggers) whose job was to assist the aerial applicator by marking specific locations to begin and end specific spraying events. Historical records indicate that the 1966 spray campaign consisted of the aerial application of 116 plots in 3 consecutive 12 hour days. It was therefore assumed that approximately 38 plots per day (116/3) were sprayed. A total of 45 plots were identified as being sprayed with either Agent Orange, Agent Purple or some other mixture containing 2,4,5-T, each of which contained some level of 2,3,7,8-Tetrachloro-p-dioxin (TCCD) as a contaminant. It was assumed that all 45 plot (receiving either Agent Orange, Purple or some other mixture containing 2,4,5-T) were sprayed within a given day.

A pair of flaggers was assumed to "flag" all 45 plots within a given 12 hour shift. The 1967 spray campaign consisted of spraying 37 plots. Seven plots were sprayed with herbicide mixtures potentially contaminated with PCDD while and additional 18 plots were sprayed with mixtures containing HCB. Although fewer plots were sprayed in 1967 compared to the 1966 campaign, the amount of time each receptor was assumed to spend on each plot in 1967 remained unchanged from the 1966 campaign. Refer to Tables 5-4 through 5-7 for the number of plots containing either PCDD or HCB in both the 1966 and 1967 spray campaigns.

Exposure of the flagger to PCDD and HCB was assumed to occur during routine flagging activities through the inhalation of vapours and dermal absorption through skin. An accidental scenario was also evaluated in which the flagger experiences an additional dermal exposure

event as a result of receiving a direct spray of the chemical mixture with the highest concentration of PCDD or HCB. Exposures as a result of both the routine and accidental exposure scenarios are described below.

Section 5.4.3.1 describes the methodology used to predict exposure to the flagger under the routine exposure scenario using PHED UEs. While this approach is widely accepted and endorsed by reputable agencies, some uncertainty exists in respect to the level of training provided to individuals involved in the 1966 and 1967 trials. Generally, use of the PHED UEs assumes that individuals involved in flagging activities are professionally trained. Therefore, an alternate approach for estimating exposure to flaggers is provided in Section 5.4.3.3 in which more conservative assumptions are adopted.

5.4.3.1 Exposure Resulting from Routine Flagging Activities

Exposure estimates for a flagger were based on PHED UEs for aerial application of liquid herbicides. It was assumed that an individual was involved in the flagging of all plots receiving chemical mixtures during the 1966 and 1967 trials. Exposure occurred as a result of absorption through both dermal and inhalation routes. As described previously, UEs for three levels of PPE were included in the assessment (Table 5-10). When using the PHED approach to predict exposures of individuals to herbicide mixtures, body weight (70.7 kg as per Health Canada, 2004a) was the only receptor-specific input parameter required. In other words, the PHED approach expresses dermal exposure (for routine activities) as a function of application rate, area treated, dermal units (refer to Table 5-10) and the proportion of applied dose absorbed through the skin. A body weight of 70.7kg remained constant for all exposure levels (*i.e.,* low, central and, high).

Table 5-10 PHED Unit Exposure Values for the Flagger for Low, Central, and High Exposure Estimates (mg/lb chemical handled)

Exposure Level	Dermal Exposure				Inhalation Exposure
	Clothing Scenario	Body Exposure	Hand Exposure	Total Dermal Exposure	
Low	Coveralls over single layer with gloves	7.07E-03	2.72E-04	7.34E-03	2.36E-04
Central	Single layer with gloves	8.38E-03	2.72E-04	8.65E-03	3.76E-04
High	Single layer without gloves	8.38E-03	2.73E-03	1.11E-02	

Using the PHED UEs presented in Table 5-10, and the application rates presented in Tables 5-4 to 5-7, the dermal and inhalation exposures were calculated as follows:

Equation 10

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

where:

$EXP_{Dermal\ Routine}$	=	Dermal exposure through routine activities (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Acres Treated per day (acres/day)
UE_{Dermal}	=	Dermal Unit exposure (mg/lb chemical handled)
P	=	Proportion of applied dermal dose absorbed (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

and

Equation 11

$$EXP_{Inhal\ Routine} = \frac{AR \times AT \times UE_{Inhal} \times CF \times IAF}{BW}$$

where:

EXP_{Inhal}	=	Inhalation exposure through routine activities (ng/kg bw/day)
AR	=	Application Rate (lbs/acre)
AT	=	Acres Treated per day (acres/day)
UE_{Inhal}	=	Inhalation Unit exposure (mg/lb handled)
IAF	=	Inhalation Absorption Factor (chemical specific) (unitless)
CF	=	Conversion factor of 1.0 x 10^6 ng/mg
BW	=	Body Weight (kg)

In the above equations, the proportion of applied PCDD or HCB absorbed through the skin (P) was based on an exposure duration of the entire 12-hour shift. Dermal exposure estimates from each of the plots were added together to generate a total absorbed dose resulting from one 12-hour shift.

5.4.3.2 Exposure Resulting from Accidental Spraying

An accident scenario was developed for the flagger which assumed that an individual was directly sprayed with 2.7 times the plot-specific application rate. Based on the results of a 1964 calibration trial cited by REMSpC (2006), individuals standing within the aerial flight path could, depending on the wind speed and direction, receive an application rate of up to 2.7 times the intended application rate. A limited modeling exercise conducted by REMSpC (2006) indicated that peak factors of up to 1.4 may have occurred during the 1966 trials. Because of the limit data incorporated into the modeling exercise, it was decided to employ data from the 1964 test trials and, therefore, a value of 2.7 was used in both the 1966 and 1967 scenarios. The test plots containing the highest PCDD and HCB application rates were identified and selected for the accident scenario. The forest canopy intercept fraction was assumed to be zero for the accident scenario and, therefore, the area of exposed skin would have come into direct contact with 2.7 times the PCDD or HCB plot-specific application rate. The accident was assumed to occur once within a 12-hour shift using the input parameters presented in Table 5-11 as follows:

Equation 12

$$EXP_{accident} = \frac{AES}{BW} \times \left(2.7 \times AR \times CF_I\right) \times P \times CF_{II}$$

where:

$EXP_{accident}$	=	Dermal exposure through accidental dermal contact with aerial spray (ng/kg bw/event) during an accident scenario
AES	=	Area of exposed skin (cm^2)
BW	=	Body weight (kg)
AR	=	Contaminant application rate (g/m^2)
CF_I	=	Conversion factor (1,000mg/g/10,000cm^2/m^2 = 0.1 mg m^2 /g cm^2)
CF_{II}	=	Conversion factor 1.0 x 10^6 ng/mg
P	=	Proportion of applied dermal dose absorbed (unitless)
2.7	=	Worst-case multiplier based on wind speed and direction

Table 5-11 Exposure Input Parameter for the Flagger and Accidental Exposure Scenarios

Receptor Parameter	Units	Exposure Estimate	Value	Reference
Body Weight (kg)	kg		70.7	Health Canada, 2004a
Surface Area of Exposed Skin[a]	(cm^b/event)	low	5,230	(U.S. EPA, 1997)
		central	9,350	(U.S. EPA,1997)
		high	15,040	(U.S. EPA,1997)
Duration of Exposure Event	hrs/plot	-	0.27	Based on 45 plots per 12 hour day
Canopy Intercept Fraction	unitless	low	0.9	Karch *et al*., 2004
		central	0.8	Karch *et al*., 2004
		high	0.7	Karch *et al*., 2004
Canopy Intercept Fraction – Accident Scenario	unitless	-	0.0	Assumed
Chemical-Specific Parameters				
PCDD first-order dermal absorption rates	hr^{-a}	low	0.004	Calculated based on SERA (2001)
		central	0.019	
		high	0.094	
HCB first-order dermal absorption rates	hr^{-a}	low	0.004	
		central	0.017	
		high	0.069	
Proportion of PCDD absorbed over period	unitless	low	0.001	
		central	0.005	
		high	0.025	
Proportion of HCB absorbed over period	unitless	low	0.001	
		central	0.005	
		high	0.02	

[a] Unlike other scenarios, skin surface areas from the U.S. EPA Exposure Factor Handbook were used for the Flagger Scenario because this source reported the area of the head and trunk. These data were required when considering a spray event. The Health Canada PQRA only reports the area of the hand, arms and legs.

[b] The intercept fraction (IF) represents the proportion of the aerial deposition rate which is captured by the forest canopy prior to reaching the forest floor. The proportion of the initial deposition rate which would make contact with the forest floor would be equal to 1 – IF; therefore, the lower the IF value the greater the deposition reaching the forest floor will be.

For a detailed discussion regarding the dermal absorption methods used by SERA (2001), refer to Section 5.3.1.2.

5.4.3.3 Alternate Exposure Assessment Methodology for Routine Flagging Activities

As described in Section 5.4.3.1, PHED data were used in combination with site-specific application rates to provide quantitative exposure estimates for an individual flagging under an aerial herbicide application scenario. The following describes an alternate approach used to quantify exposures under the same general flagging scenario. The alternate approach used the methods provided by ENSR (2005) and the USDA Forest Service (2003).

It was assumed that the forest canopy intercepted a large proportion of the aerial application rate prior reaching a flagger. According to historical records, the forest canopies of the test plots were extremely dense. Based on information provided by Karch *et al.* (2004), a dense canopy was able to intercept between 70% and 90% of the original aerial spray application. As a result, the current assessment used a low, central and high intercept fraction of 0.7, 0.8 and, 0.90, respectively.

As previously indicated, some exposure parameters were characterized using a range of data, defined by 3 individual estimates including high, low and central approximations. The area of exposed skin assumed to come into direct contact with aerial spray was characterized under these three exposure levels. As a worst-case, the head, legs (upper and lower), arms (upper and lower) and trunk (including the neck) was assumed to come into direct contact with aerial deposition. Although the trunk was likely be covered, it was considered plausible under a worst-case scenario that aerial spray could deposit on a single layer of clothes and penetrate onto the skin. The central approximation assumed the head, upper and lower arms and legs to be exposed, while the lower case scenario only assumed that the head, lower arms and legs were exposed. Refer to Table 5-11 for exposed body surface areas.

It was assumed a flagger completed all 45 plots in one 12 hour shift. It was also assumed that the flagger came into direct dermal contact with the aerial application rates (minus the canopy intercept) at each plot. As a result, the flagger was in contact with the aerial deposition for approximately 16 minutes per plot. In other words, the flagger was assumed to be in direct contact with various herbicide mixtures for his/her entire 12-hour shift. Exposure under this scenario was calculated as follows:

Equation 13

$$EXP_{Alternate\,Routine} = \frac{AES}{BW} \times \left(AR \times CF_I \times \left(1 - CIF\right)\right) \times P \times CF_{II}$$

where:

$EXP_{Alternate\ Routine}$	=	Dermal exposure through routine dermal contact with aerial spray (ng/kg bw/event) during routine work
AES	=	Area of exposed skin (cm^2)
BW	=	Body weight (kg)
AR	=	Contaminant application rate (g/m^2)
CF_I	=	Conversion factor (1,000mg/g/10,000cm^2/m^2 = 0.1 mg m^2 /g cm^2)
CF_{II}	=	Conversion factor (1.0 x 10^6 ng/mg)
CIF	=	Forest canopy intercept fraction (unitless)
P	=	Proportion of applied dermal dose absorbed (unitless)

Dermal exposure estimates from each of the plots were added together to generate a total absorbed dose resulting from one 12-hour shift.

5.4.4 Field Scout

Additional exposure to military personnel may have occurred upon re-entry to plots which had recently been sprayed. The field scout exposure scenario follows the same general approach used by the USDA Forest Service (2003) when assessing the dermal exposure from contact with contaminated vegetation. This exposure scenario assumes that a military field scout re-enters a plot which has recently been sprayed and comes into direct dermal contact with contaminated vegetation and/or other impacted surfaces. The exposure scenario uses an estimate of dislodgeable residue and rates of transfer from contaminated vegetation to skin surfaces. As per the USDA Forest Service (2003), a fraction of dislodged residue of 0.1 was used in combination with the plot-specific application rates and the transfer rate given below to help approximate the applied dermal dose.

Equation 14

$$Tr = 10^{(1.09 \times \log_{10}(Dr \times Cv) + 0.05)} \times \frac{1}{1000}$$

where:

Tr	=	Transfer rate from vegetation to skin (mg/cm^2 hr)
Dr	=	Dislodgeable residue (application rate (g/m^2) x 0.1)
Cv	=	Conversion factor (100 µg/g x m^2/cm^2)

Based on the fraction of dislodged residue, the plot-specific application rate, the transfer rate, the area of exposed skin and the proportion absorbed through the skin, an absorbed dose was estimated for each of the 45 plots. As with the flagger, it was assumed that a scout made his/her way through all 45 plots in one 12-hour shift and, therefore, spent approximately 16 minutes per plot while in direct dermal contact with contaminated vegetation. The sum of all 45 plots was used as an estimate of the daily absorbed dose. The exposure parameters presented in Table 5-12 were used to approximate the absorbed dose experienced at each plot as a result of direct dermal contact with contaminated vegetation as follows:

Equation 15

$$EXP = \frac{Tr \times Tc \times ESA \times P \times CF}{BW}$$

where:

EXP	=	Absorbed dose of PCDD or HCB *via* dermal contact skin (ng/kg/plot)
Tc	=	Contact time with contaminated vegetation (hr/plot)
Tr	=	Chemical-specific transfer rate from vegetation to skin (mg/cm^2 hr)
ESA	=	Area of exposed skin (cm^2)
P	=	Proportion of applied dermal dose absorbed (unitless)
CF	=	Conversion factor (1.0×10^6 ng/mg)
BW	=	Body weight (kg)

Exposure estimates were generated for each plot. The sum of all plots potentially containing PCDD or HCB was summed to generate a total exposure estimate. The time period assumed between initial spray operations and re-entry into each plot was short enough to ensure that the liquid carrier had not evaporated from the vegetation.

Table 5-12 Exposure Input Parameter for Field Scout Scenario

Receptor Parameter	Units	Exposure Estimate	Value	Reference
Body Weight (kg)	kg		70.7	Health Canada, 2004a
Surface Area of Exposed Skin	(cm^2/event)	low[b]	2500	Health Canada, 2004a
		central[a]	3390	Health Canada, 2004a
		high[c]	9110	Health Canada, 2004a
Duration of Exposure Event	hrs/plot	-	0.27	Assumed based on 45 plots per 12 hour day
Contact Time	hrs/plot	-	0.27	Assumed based on 45 plots per 12 hour day
Proportion Dislodged	unitless	-	0.1	USDA Forest Service (2003)
Chemical-Specific Parameters				
PCDD first-order dermal absorption rates	hr^{-1}	low	0.004	Calculated based on SERA (2001)
		central	0.019	
		high	0.094	
HCB first-order dermal absorption rates	hr^{-1}	low	0.004	
		central	0.017	
		high	0.069	
Proportion of PCDD absorbed over period (T)	unitless	low	0.0001	
		central	0.005	
		high	0.025	
Proportion of HCB absorbed over period (T)	unitless	low	0.001	
		central	0.005	
		high	0.02	

[a] Assumes that arms and hands are available for direct contact with vegetation
[b] Assumes that only the arms are available for direct contact with vegetation
[c] Assumes that arms, legs and hands are available for direct contact.

For a detailed discussion regarding the dermal absorption methods used by SERA (2001), refer to Section 5.3.1.2.

5.4.5 Military Trainee

Historical records indicate that lands affected by herbicide applications may have been used for training military personnel. These receptors may have spent extended periods of time training within these areas. The 1966 spray campaign was completed between June 14th and June 16th. It was assumed that military training operations commenced the following year on the exact plot locations of the 1966 spray campaign. Military Trainees were assumed to spend 2 months of the year at the 1966 spray campaign site. The exposure duration of 2 months was kept constant for low, central and high-end exposure estimates. The 1967 spray campaign consisted of 37 plots. Seven plots were sprayed with herbicide mixtures potentially contaminated with PCDD while an additional 18 plots were sprayed with mixtures containing HCB. During this time, individuals were assumed to come into contact with contaminants of concern *via* three main exposure pathways, including: incidental soil/dust ingestion, direct dermal contact with surface soils and ingestion of wild berries. Because it is impossible to know which plots a Military Trainee may come into contact with over a prolonged period of time, a chronic exposure rate (expressed on a ng/kg bw/day basis) was predicted for each plot sprayed with herbicide mixtures potentially containing PCDD and/or HCB. Because it cannot be determined with any certainty where (within each spray area) Military Training may have occurred, the mean exposure estimates (*i.e.,* low, central and high) from all plots (potentially contaminated with PCDD and/or HCB) were used to represent long-term daily intake rates.

PCDD and HCB concentrations in surface soil were predicted using methods provided by the U.S. EPA Risk Assessment Protocol for Hazardous Waste Combustion Facilities (U.S. EPA, 2005) in combination with various estimates of chemical-specific soil-half life data and the first-order rate law. Refer to Table 5-13 for the range of soil-half life values used for TCDD and HCB.

As per U.S. EPA (2005), a soil mixing zone of 1 cm was assumed for soils that maybe available for direct contact (*i.e.,* incidental soil ingestion and/or dermal contact) while a mixing zone of 20 cm was used to represent the root-zone of wild plants. Concentrations of PCDD and HCB in surface soil (at 1cm and 20cm in depth) were predicted at each plot one year after the initial spray campaigns. As previously indicated, a range of forest canopy intercept fractions were used in the derivation of predicting contaminant soil concentrations. Concentrations of PCDD and HCB in wild berries were derived using predicted root zone soil concentrations and soil-plant bio-transfer factors provided by RAIS (2006). The following equations were used to predict soil concentration under the forest canopy one year after the initial spray campaign.

Equation 16

$$Soil_{conc} = \frac{DEP}{BD \times MZ} \times FCI \times CF$$

where:

$Soil_{conc}$	=	Initial soil concentration immediately after spray event (ng/g)
DEP	=	Application rate of PCDD or HCB (g/m^2)
BD	=	Soil bulk density (1,500 kg/m^3)
MZ	=	Soil mixing zone (0.01 m for direct contact; 0.20 m root zone)
FCI	=	Fraction of application rate making contact with forest floor (unitless)

CF = Conversion factor (1.0E+06 ng/g x kg/g)

Equation 17

$$Soil_{1\,year} = Soil_{conc} \times e^{-kt}$$

where:

$Soil_{1\ year}$ = Soil concentration 1 year after spray event (ng/g)
k = Soil loss constant for PCDD and HCB in soil ($years^{-1}$)
t = 1 year.

Equation 18

$$k = \frac{\ln 2}{t_{1/2}}$$

Where:
$t_{1/2}$ = Chemical-specific half-life values of PCDD or HCB in soil (years);

Table 5-13 Half Life of TCDD and HCB in Surface Soil

	half life (years)			Reference
	Low	central	high	
TCDD	1	2	3	JW, 2006; Mackay *et al*., 1992a
HCB	2.7	6	7.5	JW, 2006; Mackay *et al*., 1992b

Concentrations of PCDD and HCB in wild berries were derived using the predicted soil concentration within the root zone (assuming a 20 cm mixing zone) and soil-to-plant transfer factors. Refer to Appendix E for the predicted soil and wild berry PCDD concentrations at each plot. The following equation was used to predict exposures of the Trainee to PCDD and HCB as a result of consuming wild berries:

Equation 19

$$EXP_{berries} = \frac{Soil_{1\,year} \times BTF \times WBC \times Bio_{gut} \times EF \times ED}{AT}$$

where:

$EXP_{berries}$ = Absorbed dose from the consumption of wild berries (ng TEQ/kg bw/d)
$Soil_{1year}$ = Soil concentration 1 year after application (ng/g)
BTF = Soil-to-plant uptake factor (unitless)
WBC = Wild berry consumption rate (g/kg bw/d)
Bio_{gut} = bioavailability TCDD or HCB in the gut (unitless; a value of 0.9 was utilized based on U.S. EPA, 2003)
EF = Exposure frequency (d/years)
ED = Exposure duration (years)
AT = Averaging time (days)

Military Trainees were assumed to spend time on the same areas that had been sprayed in the previous year. An incidental soil ingestion rate for construction workers of 100 mg/d as reported by Health Canada (2004a) was used to characterize the soil intake rate characteristics of a Military Trainee while spending time in this area. A gut bioaccessibility factor for PCDD in soils and a study bioavailability were both used (as illustrated in the equation below) to predict an absorbed dose resulting from incidental soil ingestion. As indicated by Ruby *et al.* (2002), the bioaccessibility of PCDD in soils is much less than that in other media (*e.g.,* food).

Equation 20

$$EXP_{soil} = \frac{Soil_{1\,year} \times SI \times Bio_{soil} \times Bio_{gut} \times EF \times ED}{AT \times BW}$$

where:

EXP_{soil}	=	Absorbed dose *via* incidental soil ingestion (ng TEQ/kg bw/d)
$Soil_{1year}$	=	Soil concentration 1 year after application (ng/g)
Bio_{soil}	=	Soil bioaccessibility factor (unitless)
Bio_{gut}	=	Study bioavailability TCDD or HCB in the gut (unitless)
SI	=	Incidental soil ingestion rate (g/d)
EF	=	Exposure frequency (d/years)
ED	=	Exposure duration (years)
AT	=	Averaging time (days)
BW	=	Body weight (kg)

In addition to the incidental ingestion of soil and consumption of wild berries, Military Trainees were assumed to come into direct dermal contact with soils which may have received aerial deposition during the 1966/1967 spray campaigns. As a result, exposures *via* the direct dermal contact with impacted soils were evaluated through the use of the following exposure equation:

Equation 21

$$EXP_{soil} = \frac{Soil_{1\,year} \times \left(\left(AH \times AFH\right) + \left(AB \times AFB\right)\right) \times EPD \times DAF \times EF \times ED}{AT \times BW}$$

where:

EXP_{dermal}	=	Absorbed dose from direct dermal contact with soil (ng TEQ/kg bw/d)
$Soil_{1year}$	=	Soil concentration 1 year after application (ng/g)
AH	=	Surface area of hands (cm^2)
AFH	=	Soil adherence factor – hands (g/cm^2 – event)
AB	=	Surface area of exposed body (cm^2)
AFB	=	Soil adherence factor – body (g/cm^2 – event)
EPD	=	events per day (events/day)
DAF	=	Dermal absorption factor (unitless)
EF	=	Exposure frequency (d/years)
ED	=	Exposure duration (years)

AT = Averaging time (days)
BW = Body weight (kg)

Table 5-14 contains a summary of exposure parameters and assumptions used in the military Trainee exposure scenario.

Table 5-14 Exposure Input Parameter for On-Site Military Trainee Scenario

Receptor Parameter	Units	Description	Value	Reference
Body weight (kg)	kg		70.7	Health Canada, 2004a
Surface area of exposed skin	(cm^b)	Hands	890	Health Canada, 2004a
		Body	9110	Health Canada, 2004a
Incidental soil ingestion rate	g/d	-	0.1	Health Canada, 2004a
Soil adherence factor	g/cm^2 – event	Hands	0.001	Health Canada, 2004a
		Body	0.0001	Health Canada, 2004a
Consumption rate of wild berries[a]	g/kg bw/d	-	0.14	Derived - based on Dietary Survey conducted in Northern Ontario
Exposure frequency	d/years	-	60	Assumed
Exposure Duration	years	-	3.0	Assumed
Averaging time[2]	d	-	1095	Assumed
Chemical-Specific Parameters				
Soil bioaccessibility Factor – TCDD	unitless	-	0.34	Ruby *et al.*, 2002
Soil bioaccessibility Factor – HCB	unitless	-	0.34	Assumed to be the same as TCDD
Study Bioavailability – TCDD	unitless	-	0.9	U.S. EPA, 2003; absorbed dose after ingestion with corn oil
Study Bioavailability – HCB	unitless	-	0.85	Schlummer *et al.*, 1998
Dermal absorption factor from soil – TCDD	unitless	-	0.01	Shu *et.al.*, 1988
Dermal absorption factor from soil - HCB	unitless	-	0.1	U.S. EPA (2003)
Soil-Plant Uptake Factor - TCDD	unitless	-	0.0009	RAIS, 2006; McKone, 1994
Soil-Plant Uptake Factor - HCB	unitless	-	0.0065	RAIS, 2006; McKone, 1994
Forest canopy intercept fraction[c]	unitless	low	0.9	Karch *et al.*, 2004
		central	0.8	Karch *et al.*, 2004
		high	0.7	Karch *et al.*, 2004

[a] The wild berry consumption rate represents the average daily consumption rate of an individual over the course of the exposure duration. It is plausible that an individual could eat more (or less) berries than the average on any given day, but over the course of the exposure duration, it was assumed the average daily intake to be 0.14 g/kg/day.

[b] For non-carcinogenic substances the averaging time is set equal to the exposure duration. 1095 days is equivalent to 3 years.

[c] The intercept fraction (IF) represents the proportion of the aerial deposition rate which is captured by the forest canopy prior to reaching the forest floor. The proportion of the initial deposition rate which would make contact with the forest floor would be equal to 1 – IF; therefore, the lower the IF value the greater the deposition reaching the forest floor will be.

It was also assumed that the military trainee might have received exposure through an accident scenario, similar to that which was developed for the flagger. This scenario assumed that an individual was directly sprayed with 2.7 times the plot-specific application rate. The test plots containing the highest PCDD and HCB application rates were identified and selected for the accident scenario. The forest canopy intercept fraction was assumed to be zero for the accident

scenario and, therefore, the area of exposed skin came into direct contact with 2.7 times the PCDD or HCB plot-specific application rate. The accident was assumed to occur once.

5.5 Exposure Estimates

A total of 45 plots were identified as being sprayed in 1966 with either Agent Orange, Agent Purple or some other mixture containing 2,4,5-T, each of which contained some level of PCDD as a contaminant. It was assumed that all 45 plots (receiving either Agent Orange, Purple or some other mixture containing 2,4,5-T in 1966) were sprayed within a single day. Because each plot potentially received a different herbicide mixture and/or application rate, routine exposure estimates of all receptor groups were therefore calculated on a plot-by-plot basis. With the exception of the Military Trainee, the sum of exposure estimates from each plot was used to derive the estimated daily exposure rate of a specific receptor group. Refer to Appendix E (the 'Worked Example') for a list PCDD exposure estimates per plot during the 1966 spray campaign.

An accident scenario was assumed to occur once within a 12-hour shift and, therefore, accidental exposure estimates conservatively employed data from those plots which contained the highest PCDD and/or HCB application rates. With the exception of the Trainee, each dioxin exposure estimate represents an absorbed dose resulting from a one-day exposure event. Estimated exposures to PCDD TEQ and HCB for each of the five receptor groups under the exposure scenarios described above are presented in Sections 5.5.1 to 5.5.5.

5.5.1 Exposure Estimates for the Mixer/Loader

The predicted dermal and inhalation exposures for the mixer/loader exposed to PCDD and HCB at the low, central and high exposure levels are presented in Table 5-15. As described in Section 5.3.1, the low, central and high exposure estimates for the mixer/loader were distinguished from one another by the use of a range in values for a number of exposure parameters. Exposure estimates are separated for the 1966 and 1967 trials. As previously discussed, the 1967 spray campaign was smaller than that of 1966. Secondly, Agent Purple (which contains higher levels of PCDD relative to Agent Orange) was not sprayed in 1967. As a result, exposure predictions of the Mixer/Loader to PCDD TEQ are lower in 1967 relative to 1966 estimates. Within each trial year, exposures associated with the routine exposure scenario and the accidental exposure scenario are presented both independently and combined.

5.5.2 Exposure Estimates for the Applicator

The predicted dermal and inhalation exposures for the applicator exposed to PCDD and HCB at the low, central and high exposure levels are presented in Table 5-16. As described in Section 5.3.1, the low, central and high exposure estimates for the applicator were distinguished from one another by the use of a range in values for a number of exposure parameters including the estimated PCDD content of the herbicidal active ingredient, the rate of dermal absorption, and the level of personal protective equipment utilized during the application. As with the Mixer/Loader, the PCDD TEQ exposure estimates in 1967 are lower relative to 1966 due to the smaller number of plots sprayed and absence of Agent Purple in 1967. Exposure estimates are separated for the 1966 and 1967 trials.

5.5.3 Exposure Estimates for the Flagger

The predicted dermal and inhalation exposures for the flagger exposed to PCDD and HCB at the low, central and high exposure levels are presented in Table 5-17. As described in Section 5.3.1, the low, central and high exposure estimates for the flagger were distinguished from one another by the use of a range in values for a number of exposure parameters including the estimated PCDD content of the herbicidal active ingredient, the rate of dermal absorption, and the level of personal protective equipment utilized during the flagging activities. Exposure estimates are separated for the 1966 and 1967 trials. Within each trial year, exposures associated with the routine exposure scenario and the accidental exposure scenario are presented both independently and combined.

Results for the flagger using the alternate exposure method described in Section 5.4.3.3 are presented in Table 5-18. The exposure estimates predicted for the accidental exposure scenario are the same as those presented in Table 5-17, and only the exposure associated with the routine flagging activities that differ from the results presented above.

The difference in PCDD TEQ exposure estimates between 1966 and 1967 can be attributed to the smaller number of plots containing TCDD in 1967 and the absence of Agent Purple, which contains relatively higher concentrations of TCDD relative to Agent Orange, in the 1967 spray campaign.

Table 5-15 Predicted Exposures to PCDD and HCB for the Mixer/Loaderunder the Routine and Accidental Exposure Scenarios (ng/kg bw/day)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
Routine 1966	2.1E-03	3.5E-02	4.2E+01	1.0E-01	3.4E-01	6.7E-01	1.1E-01	3.7E-01	4.3E+01
Accident 1966	6.6E+01	6.5E+02	4.4E+03	-	-	-	6.6E+01	6.5E+02	4.4E+03
Total 1966	6.6E+01	6.5E+02	4.4E+03	1.0E-01	3.4E-01	6.7E-01	6.6E+01	6.5E+02	4.4E+03
Routine 1967	5.1E-05	2.3E-03	8.5E+00	2.2E-03	1.9E-02	1.2E-01	0.0E+00	2.0E-02	8.6E+00
Accident 1967	3.7E+00	7.9E+01	1.9E+03	-	-	-	3.7E+00	7.9E+01	1.9E+03
Total 1967	3.7E+00	7.9E+01	1.9E+03	2.2E-03	1.9E-02	1.2E-01	3.7E+00	7.9E+01	1.9E+03
HCB									
Routine 1966	3.4E-03	2.2E-02	1.1E+01	1.5E-01	2.3E-01	2.3E-01	1.5E-01	2.5E-01	1.1E+01
Accident 1966	8.4E+01	3.4E+02	1.4E+03	-	-	-	8.4E+01	3.4E+02	1.4E+03
Total 1966	8.4E+01	3.4E+02	1.4E+03	1.5E-01	2.3E-01	2.3E-01	8.4E+01	3.4E+02	1.4E+03
Routine 1967	8.1E-03	5.2E-02	2.6E+01	3.5E-01	5.5E-01	5.5E-01	3.6E-01	6.0E-01	2.6E+01
Accident 1967	1.7E+02	6.9E+02	2.7E+03	-	-	-	1.7E+02	6.9E+02	2.7E+03
Total 1967	1.7E+02	6.9E+02	2.8E+03	3.5E-01	5.5E-01	5.5E-01	1.7E+02	6.9E+02	2.8E+03

Table 5-16 Predicted Exposures to PCDD and HCB for the Applicator (ng/kg bw/day)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
1966	4.5E-04	7.3E-03	6.5E-02	4.5E-03	1.5E-02	3.0E-02	5.0E-03	2.2E-02	9.5E-02
1967	1.1E-05	4.8E-04	1.3E-02	9.5E-05	8.5E-04	5.1E-03	0.0E+00	1.0E-03	1.8E-02
HCB									
1966	7.4E-04	4.6E-03	1.7E-02	6.5E-03	1.0E-02	1.0E-02	7.0E-03	1.5E-02	2.7E-02
1967	1.8E-03	1.1E-02	3.9E-02	1.5E-02	2.4E-02	2.4E-02	1.7E-02	3.5E-02	6.3E-02

Table 5-17 Predicted Exposures to PCDD and HCB for the Flagger under the Routine and Accidental Exposure Scenario (ng/kg bw/day)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
Routine 1966	1.0E-03	1.3E-02	1.7E-01	3.3E-02	1.1E-01	2.2E-01	3.5E-02	1.3E-01	3.9E-01
Accident 1966	1.2E+00	2.1E+01	2.3E+02	-	-	-	1.2E+00	2.1E+01	2.3E+02
Total 1966	1.2E+00	2.1E+01	2.3E+02	3.3E-02	1.1E-01	2.2E-01	1.2E+00	2.1E+01	2.3E+02
Routine 1967	2.2E-05	7.4E-04	2.9E-02	7.1E-04	6.4E-03	3.9E-02	7.3E-04	7.1E-03	6.8E-02
Accident 1967	5.8E-02	2.2E+00	8.7E+01	-	-	-	5.8E-02	2.2E+00	8.7E+01
Total 1967	5.8E-02	2.2E+00	8.7E+01	7.1E-04	6.4E-03	3.9E-02	5.9E-02	2.2E+00	8.7E+01
HCB									
Routine 1966	2.0E-03	8.0E-03	4.2E-02	4.8E-02	7.7E-02	7.7E-02	5.0E-02	8.5E-02	1.2E-01
Accident 1966	1.0E+00	7.4E+00	4.7E+01	-	-	-	1.0E+00	7.4E+00	4.7E+01
Total 1966	0.0E+00	7.4E+00	4.7E+01	4.8E-02	7.7E-02	7.7E-02	1.1E+00	7.5E+00	4.8E+01
Routine 1967	4.0E-03	1.9E-02	9.9E-02	1.2E-01	1.8E-01	1.8E-01	1.2E-01	2.0E-01	2.8E-01
Accident 1967	3.0E+00	2.2E+01	1.4E+02	-	-	-	3.0E+00	2.2E+01	1.4E+02
Total 1967	3.0E+00	2.2E+01	1.4E+02	1.2E-01	1.8E-01	1.8E-01	3.2E+00	2.2E+01	1.4E+02

Table 5-18 Predicted Exposures to PCDD and HCB for the Flagger Exposure Scenario (ng/kg bw/day) – Alternate Method

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
Routine 1966	3.0E-01	1.1E+01	2.7E+02	-	-	-	3.0E-01	1.1E+01	2.7E+02
Accident 1966	1.2E+00	2.1E+01	2.3E+02	-	-	-	1.2E+00	2.1E+01	2.3E+02
Total 1966	1.5E+00	3.2E+01	5.0E+02	-	-	-	1.5E+00	3.2E+01	5.0E+02
Routine 1967	5.8E-03	6.0E-01	4.4E+01	-	-	-	5.8E-03	6.0E-01	4.4E+01
Accident 1967	5.8E-02	2.2E+00	8.7E+01	-	-	-	5.8E-02	2.2E+00	8.7E+01
Total 1967	6.4E-02	2.8E+00	1.3E+02	-	-	-	6.4E-02	2.8E+00	1.3E+02
HCB									
Routine 1966	4.9E-01	7.2E+00	6.9E+01	-	-	-	4.9E-01	7.2E+00	6.9E+01
Accident 1966	1.0E+00	7.4E+00	4.7E+01	-	-	-	1.0E+00	7.4E+00	4.7E+01
Total 1966	1.5E+00	1.5E+01	1.2E+02	-	-	-	1.5E+00	1.5E+01	1.2E+02
Routine 1967	1.1E+00	1.6E+01	1.5E+02	-	-	-	1.1E+00	1.6E+01	1.5E+02
Accident 1967	3.0E+00	2.2E+01	1.4E+02	-	-	-	3.0E+00	2.2E+01	1.4E+02
Total 1967	4.1E+00	3.8E+01	2.9E+02	-	-	-	4.1E+00	3.8E+01	2.9E+02

5.5.4 Exposure Estimates for the Field Scout

The field scout exposure scenario follows the same general approach used by the USDA Forest Service (2003) when assessing the dermal exposure from contact with contaminated vegetation. This exposure scenario assumed that a military field scout re-enters a plot which has recently been sprayed and comes into direct dermal contact with contaminated vegetation and/or other impacted surfaces. It is noted that the liquid herbicide mixture is assumed to be covering vegetation at the time the field scout re-enters the plot and, therefore, the scout was assumed to come into direct dermal contact with the herbicide mixture. Table 5-19 summarizes the predicted acute exposures experienced by a field scout receptor.

Table 5-19 Predicted Exposures to PCDD and HCB for the Field Scout Exposure Scenario (ng/kg bw/day)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
1966	2.0E-02	3.2E-01	8.6E+00	-	-	-	2.0E-02	3.2E-01	8.6E+00
1967	3.2E-04	1.4E-02	1.3E+00	-	-	-	3.2E-04	1.4E-02	1.3E+00
HCB									
1966	3.0E-02	1.9E-01	2.1E+00	-	-	-	3.0E-02	1.9E-01	2.1E+00
1967	8.0E-02	4.5E-01	4.9E+00	-	-	-	8.0E-02	4.5E-01	4.9E+00

5.5.5 Exposure Estimates for the Military Trainee

Military Trainees were assumed to spend 2 months of the year at the spray campaign sites. During this time, individuals were assumed to come into contact with contaminants of concern *via* three main exposure pathways, including: incidental soil/dust ingestion, direct dermal contact with surface soils and ingestion of wild berries only. Table 5-20 summarizes the predicted long-term exposure estimates associated with training in the 1966 and 1967 spray campaign plots.

Table 5-20 Predicted Exposures to PCDD and HCB for the Military Trainee (ng/kg bw/day)

Chemical	Exposure *via* Direct Dermal Contact			Exposure *via* Incidental Soil Ingestion and Wild Berry Consumption			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
PCDD									
1966	1.3E-06	7.5E-06	2.5E-05	2.2E-06	1.3E-05	4.3E-05	3.5E-06	2.0E-05	6.9E-05
1967	1.6E-07	2.5E-06	2.6E-05	2.7E-07	4.4E-06	4.5E-05	4.3E-07	6.9E-06	7.0E-05
HCB									
1966	4.9E-05	1.1E-04	1.7E-04	8.7E-06	2.0E-05	3.1E-05	5.8E-05	1.3E-04	2.0E-04
1967	1.5E-04	3.5E-04	5.4E-04	2.2E-05	5.1E-05	7.8E-05	1.8E-04	4.1E-04	6.2E-04

6.0 HAZARD ASSESSMENT

6.1 Hexachlorobenzene (HCB)

HCB is a chlorinated hydrocarbon which may contain some higher PCDFs and dioxins as impurities (Villanueva *et al.*, 1974). Health Canada has assessed HCB to be a probably human carcinogen and it has been declared toxic under CEPA. It was subsequently added to the Prohibition of Toxic Substances Regulation under CEPA in 2003. HBC registration was withdrawn in Canada in 1976 and eventually banned in 2003 (Barber *et al.*, 2005). Although HBC production has ceased in most countries, it is still generated inadvertently as a by-product and/or impurity in several chemical processes (Barber *et al.*, 2005). A substantial portion of the HCB currently measured in the atmosphere is thought to come from volatilization of old HCB in the soil from past contamination (Bailey, 2001).

The average half-life of HCB in the environment estimated from results of a number of studies is ~ 9 years (Barber *et al.*, 2005). Atmospheric degradation is extremely slow. It has been suggested that HCB in the gas phase can be transported great distances before deposition or ultimate degradation (Barber *et al.*, 2005). HCB can move around in the environment in multiple hops in a manner that has been described as the "grasshopper effect" (Barber *et al.*, 2005; Wania and Mackay, 1996). HCB is considered globally ubiquitous so some exposure is unavoidable (Barber *et al.*, 2005; USDA, 2003).

Routes of Exposure

Inhalation exposure to HCB from industrial air pollution has been linked with elevated blood levels of HCB and hepatic effects (increased porphyrins and hepatic enzymes). Incidences of human inhalation exposure have not produced the significant adverse outcomes in nursing infants that have been recorded after oral ingestion of HCB. In areas where females have received dietary exposure to HCB, consumption of mother's milk contaminated with HCB has been linked to effects on thyroid function (decreased thyroxine levels; weak evidence of hypothyroidism, goiter, and thyroid cancer), and impaired development of locomotor skills (ATSDR, 2002).

HCB may be absorbed through the skin. In experimental animals the process of dermal absorption may be relatively slow, and washing the affected area with soap significantly decreased absorption (Koizumi, 1991).

HCB Metabolism

HCB undergoes limited metabolism, yielding pentachlorophenol, tetrachloro-hydroquinone and pentachlorothiophenol as the major metabolites in urine. The acute toxicity of HCB in experimental animals was low (HSDB, 2005).

There are no detailed studies of the metabolism of HCB in humans. The available data on the systemic toxicity of HCB indicate that the pathway for the biosynthesis of haeme is a major target of HCB toxicity.

HCB is a mixed-type cytochrome P450-inducing compound, known to bind to the aryl hydrocarbon (Ah) receptor.

HCB and Cancer

HCB is a non-genotoxic carcinogen. Animal studies have demonstrated that HCB increases the risk for cancer of the liver thyroid and kidney.

The international Agency for Research on Cancer (IARC) has classified HCB as a Group 2B (possibly carcinogenic to humans) (IARC, 2001). The U.S. EPA describes HCB as Group B2 (probable human carcinogen). The American Conference of Government and Industrial Hygienists (ACGIH) have identified HCB as a confirmed animal carcinogen with unknown relevance to humans (A3).

The risk for breast cancer in humans has been investigated in relation to life-long, accumulated exposure to HCB. No evidence of a dose-response relationship for increased risk for breast cancer has been reported in a number of epidemiological studies. Chronic exposure to HCB in air was associated with thyroid cancer and increased incidence of soft tissue sarcoma.

Systemic Toxicity of HCB

The most sensitive target organs for HCB are the liver, ovary, and central nervous system. In humans, ingestion of large quantities of HCB has caused death, systemic (***e.g.***, liver, skin, bone, and thyroid), neurological, developmental, endocrine, and immunological toxicity (ATSDR, 2002).

Elevated levels of porphyrin and/or porphyrin precursors have been found in the liver, other tissues and excreta of several species of laboratory mammals. Porphyria has been reported in a number of studies in rats after subchronic or chronic oral exposure. Less frequently reported organ effects of repeated exposure to HCB include effects on the liver, lungs, kidneys, thyroid, skin and nervous and immune systems.

6.1.2 Toxicological Reference Values

Several regulatory agencies have derived TRVs for HCB. The following section provides a review of those most relevant to the current assessment. Where available, TRVs derived by Health Canada have been selected for the purpose of this assessment.

The U.S. EPA (IRIS, 1991) RfD for HCB is 0.0008 mg/kg bw/day. This RfD is based on the Arnold *et al.* (1985) 130-week feeding study in male and female rats that also included a 90-day exposure to offspring. The U.S. EPA judged the NOAEL for liver effects at a dose of 0.08 mg/kg bw/day with a LOAEL at 0.29 mg/kg bw/day. The LOAEL was characterized by U.S. EPA (1997) as "an increase ($p<0.05$) in hepatic centrilobular basophilic chromogenesis" in the offspring of the chronically exposed rats. The U.S. EPA used an uncertainty factor of 100 to derive the RfD of 0.0008 mg/kg bw/day. On the basis of evidence that when administered orally, HCB has been shown to induce tumors in the liver, thyroid and kidney, the U.S. EPA (IRIS, 1991) have also derived an oral slope factor based on the results of the Ertürk *et al.* (1986) study previously discussed. The oral slope factor, derived on the basis of hepatocellular carcinomas, is 1.6 $(mg/kg\ bw/day)^{-1}$.

Health Canada (2004b) has reported both non-carcinogenic and carcinogenic toxicity reference values for HCB. The non-cancer based tolerable daily intake was reported as 0.0005 mg/kg bw/day (0.5 µg/kg bw/day). Likewise, the cancer based slope factor has been reported as 0.83 $(mg/kg\ bw/day)^{-1}$. The slope factor is based on the tumorigenic dose $(TD)_{0.05}$ (TD_{05}- is the total intake associated with a 5% increase in incidence or mortality due to tumours scaled, where appropriate, to reflect interspecies variations (Health Canada, 1996)) value derived from the results of the Arnold *et al.* (1985) study. CEPA (1993) reports a $TD_{0.05}$ range from 0.06 mg/kg bw/day for hepatic neoplastic nodules in females to 0.17 mg/kg bw/day for parathyroid adenomas in males, which translates into slope factors ranging from 0.29 $(mg/kg\ bw/day)^{-1}$ to 0.83 $(mg/kg\ bw/day)^{-1}$ (Slope Factor = 0.05 / $TD_{0.05}$). Potency is expressed as the concentration or dose which induces a 5% increase in the incidence of, or deaths due to, tumours considered to be associated with exposure, observed in epidemiological studies in human populations or bioassays in experimental animals [Tumorigenic Dose 05 (TD_{05}) or Tumorigenic Concentration 05 (TC_{05})].

Wherever possible and if considered appropriate, information on pharmacokinetics and mechanisms is incorporated into the quantitative estimates of potency derived particularly from studies in animals (to provide relevant scaling for humans).

The data that assess effects of inhalation exposure to HCB are qualitatively and quantitatively inadequate for use in developing acute, intermediate, or chronic inhalation MRLs for HCB.

ATSDR (2002) have derived a minimal risk level (MRL) of 0.008 mg/kg bw/day for *acute-duration* oral exposure (14 days or less) for HCB. This MRL is based on a critical evaluation of a developmental study (Goldey and Taylor, 1992) that observed a lowest-observed-adverse-effect level (LOAEL) of 2.5 mg/kg bw/day for hyperactivity in offspring rats. An uncertainty factor of 300 was used (10 for extrapolation from rats to humans, 10 for human variability, and 3 for use of a minimal LOAEL). A battery of tests to demonstrate evidence of developmental neurotoxicity of HCB was assessed in off-spring (Goldey and Taylor, 1992). Evidence for hyperactivity was observed in pups treated with 2.5 or 25 mg/kg bw/day for 4 days, 2 weeks prior to mating with unexposed males. They re-oriented themselves significantly more quickly in a negative geotaxis test (on postnatal days 6 and 8), required less time in an olfactory discrimination test, and demonstrated increased exploratory activity in a motor activity test (on postnatal days 9 to 11). No significant effects on learning (swim T-maze) or motor activity (measured in older offspring on postnatal days 40 and 50, respectively) were detected. HCB exposed offspring at the 25 mg/kg bw/day dose level exhibited significantly altered acoustic startle responses (decreased at 23 days of age and increased at 90 days of age compared to controls). Thus, the study identified a LOAEL of 2.5 mg/kg bw/day for hyperactivity in the offspring rats (ATSDR, 2002).

ATSDR (2002) has derived an MRL of 0.0001 mg/kg bw/day for *intermediate-duration* oral exposure (15 to 364 days) for HCB. This MRL is based on a LOAEL of 0.01 mg/kg bw/day for minimal ovarian effects in monkeys (Babineau *et al.* 1991). An uncertainty factor of 90 was used (3 for extrapolation from monkeys to humans, 10 for human variability, and 3 for use of a minimal LOAEL) (ATSDR, 2002). Ultra-structural studies of ovaries collected from monkeys (Babineau *et al.* 1991; Bourque *et al.* 1995; Jarrell *et al.* 1993) fed doses of 0.01 to 10 mg/kg bw/day of HCB for 90 days provided the most appropriate data for development of an intermediate-duration oral MRL (ATSDR, 2002).

An MRL of 0.00005 mg/kg bw/day has been derived for *chronic-duration* oral exposure (365 days or more) for HCB (ATSDR, 2002). The chronic oral exposure MRL was based on a critical evaluation of a multigenerational study (Arnold *et al.* 1985), which observed a LOAEL of 0.016 mg/kg bw/day for hepatic effects in F_1 male rats. An uncertainty factor of 300 was used (10 for extrapolation from rats to humans, 10 for human variability, and 3 for use of a minimal LOAEL).

Selected TRVs

The non-carcinogenic and carcinogenic toxicity reference values derived by Health Canada (2004b) have been selected for the evaluation of long-term (chronic) health effects of HCB. The non-cancer based tolerable daily intake was reported as 0.0005 mg/kg bw/day (0.5 µg/kg bw/day), and the cancer based slope factor has been reported as 0.83 $(mg/kg\ bw/day)^{-1}$.

For short-term (acute) effects, the ATSDR (2002) derived MRL of 0.008 mg/kg bw/day for acute-duration oral exposure (14 days or less) for HCB was selected.

6.2 Dioxins

PCDDs and PCDFs constitute a group of highly persistent ubiquitous chlorinated organic chemicals (Haws *et al*., 2006; WHO, 2000a). They are structurally related compounds that bind to the aryl hydrocarbon receptor (AhR), the ligand-activated transcription factor, and are commonly referred to as dioxin-like compounds (DLCs). Due to their persistence, tendency to biomagnify through the food chain and their lipophilicity, once consumed they accumulate in humans potentially causing chronic lifetime human exposure. Because the mechanism of action is the same and because they are commonly found in the environment as a mixture, the Toxic Equivalency Factor (TEF) methodology has been developed. PCDDs, PCDFs and dioxin like PCBs have been assigned a TEF based on their relative potency as compared to 2,3,7,8-TCDD, which has been assigned a TEF of 1 (van den Berg *et al.,* 1998). The amount of congener present in a sample is multiplied by its TEF to give the "toxic equivalent" concentration (TEQ) for the congener expressed in terms of 2,3,7,8-TCDD. The total dioxin TEQ approach and current values have been accepted internationally as the most appropriate way to estimate the potential health risks of dioxin mixtures (Schecter *et al.*, 2006).

This report primarily focuses on TCDD, the most toxic and well studied dioxin. Where it is necessary this document refers to relevant data related to other DLCs that are essential in the development of appropriate guidelines and exposure limits. For a more detailed toxicological profile, refer to Appendix B.

6.2.1 Chronic Health Effects

A number of DLCs have demonstrated numerous toxic responses similar to the most toxic dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The effects include dermal toxicity, immunotoxicity, reproductive effects and teratogenicity, endocrine disruption and carcinogenicity (WHO, 2000a). Studies of highly exposed populations suggest various non-cancer health effects are associated with dioxin exposure; for example, chloracne (a skin condition), increases in liver enzymes, increased cardiovascular disease and developmental effects. However, most of these effects, such as chloracne, appeared only at doses several orders of magnitude greater than the general public receives from background contamination in food (JECFA, 2001).

2,3,7,8-TCDD has been shown to cause cancer in several chronic studies at multiple sites in multiple species (WHO, 2003). There is good evidence to indicate that this is the result of an initial binding to the Ah Receptor (Fischer *et al.*, 1998; U.K COC, 2001). Activation of the AhR is considered a necessary but not sufficient requirement for the toxicity of dioxins (EFSA Scientific Colloquium, 2004). Through a complex sequence of events from binding to the AhR to gene transcription, the consensus is that sufficient interaction with the AhR leads to specific cellular and tissue toxicity, the repair and regeneration of which lead secondarily to tumour formation (U.S. EPA, 2003; van Leeuwen *et al.*, 2000; WHO, 1991). The greater the amount of TCDD available to bind the AhR, the greater the number of receptor-ligand complexes. As with all other receptor-mediated biological responses, a minimum number of these complexes is needed to elicit an adverse effect, implying that there is a threshold below which adverse effects do not result (Popp *et al.*, 2006).

Dose-response curves derived from studies in laboratory animals provide strong evidence that cancer is a highly non-linear endpoint; *i.e.*, there is a threshold dose below which no tumorigenic response is observed. Recently the National Toxicology Program conducted 2-year carcinogenicity bioassays of TCDD as well as 4-pentachlorodiobenzofuran (4-PeCDF), polychlorinated biphenyl-126 (PCB) that binds to the Ah receptor, and a mixture of the three (NTP, 2004a,b,c,d). In the study of TCDD, no significant tumour response was seen for doses as high as 22 ng/kg body weight (5 days/week). The first significant response was observed at 46 ng/kg (5 days/week) again providing evidence that the dose-response for TCDD carcinogenesis is non-linear with a threshold region.

Epidemiological studies of human populations occupationally or accidentally exposed to dioxins present a mixed picture with respect to dioxins and cancer. Previously, estimates of exposures and cancer dose-response by individual scientists and regulatory/scientific bodies have all relied on cumulative exposure estimates based on back-calculations of measured levels over decades, assuming constant first-order elimination rates ranging from 7 to 9 years in adults (Flesch-Janys *et al.*, 1998; Starr, 2001; Crump *et al.,* 2003; WHO, 2001; U.S. EPA, 2003). Application of the dose-dependent elimination model to the U.S. NIOSH cohort of herbicide workers indicated that these previous dose estimates may have underestimated the maximum concentrations in these workers by several-fold to an order of magnitude or greater (Aylward *et al.*, 2005b). Accordingly, dose estimates for occupational cohorts should be re-evaluated in light of the demonstration of concentration-dependent elimination kinetics for TCDD (Aylward *et al.*, 2005a). In addition, the large degree of uncertainty in back-calculated dose estimates should be explicitly incorporated in quantitative estimates of TCDD's carcinogenic potency; for example, the cancer potency factor derived by the U.S. EPA (U.S. EPA, 2003; 2004).

6.2.2 Acute Effects

The Agency for Toxic Substances and Disease Registry (ATSDR, 1998) has compiled a series of studies that have identified levels of significant exposure to 2,3,7,8-TCDD following acute one-time exposure. These studies are outlined below:

Acute Dermal Exposure: ATSDR identified a single study that demonstrated adverse effects following one-time dermal exposure to 2,3,7,8-TCDD. A study by Schwetz *et al.* (1973) reported a dermal LD_{50} ("serious" effect) value of 275 μg/kg for rabbits. The deaths occurred 12 to 22 days post-exposure. The study by Schwetz *et al.* (1973) also reported a LOAEL of

2,000 μg for transient inflammation of conjunctiva in rabbits. This biological endpoint was classified by ATSDR (1998) as a "less serious" effect.

Acute Oral Exposure: ATSDR has identified a large number of studies that demonstrated adverse effects following a single oral exposure to 2,3,7,8-TCDD. The studies examined a variety of "serious" and "less serious" biological endpoints. The lowest exposure level associated with an adverse effect was reported to be 0.01μg/kg bw/day for immunological effects in the mouse (Burleson *et al.,* 1996). For this study, female mice were administered a single gavage dose of 2,3,7,8-TCDD in corn oil. Seven days post-exposure the mice were infected with influenza A at a dose that does not typically cause mortality. Statistically significant increases in mortality were observed for mice that had been previously exposed to 0.01 μg 2,3,7,8-TCDD/kg bw. The NOAEL for impaired resistance to influenza A virus infection was determined to be 0.005 μg/kg bw. This biological endpoint was classified by ATSDR (1998) as a "less serious" effect.

The lowest one-time oral exposure associated with a "serious" effect was reported to be 0.064 μg/kg bw. This LOAEL was derived by Mably *et al.* (1992) and considered effects of 2,3,7,8-TCDD on spermatogenesis and reproductive capability in male rats that received exposures in *utero* or during lactation.

6.2.3 Physiologically Based Pharmacokinetics (PBPK)

The elimination of TCDD in mammals is dependent upon diffusion into and out of adipose tissue, metabolism, hepatic sequestration, and hepatic elimination rate (Emond *et al.*, 2006). Recent animal studies support the participation of CYP1A2 and other CYPs in the metabolism and elimination of TCDD (Emond *et al.*, 2006).

The most recent pharmacokinetic models for TCDD describe the distribution of TCDD as diffusion limited (Andersen *et al.* 1997; Carrier *et al.,* 1995a,b; Kohn *et al.,* 1996; Wang *et al.,* 1997; 2000; Maruyama *et al.,* 2002; Emond *et al.,* 2004; Aylward *et al.,* 2005a; Emond *et al.*, 2006). Some of these models also include an inducible cytochrome P450-TCDD binding protein regulated by the Ah receptor in hepatic tissue (Diliberto *et al.,* 1996; Emond *et al.*, 2006).

Empirical models developed from epidemiological data have described the rate of elimination of TCDD on the basis of first order kinetics with half-lives varying from 7 to 8.7 years (Aylward *et al.,* 1996; Crump *et al.,* 2003; Flesch-Janys *et al.,* 1996; Steenland *et al.,* 1999). Clearance rates from the hepatic compartment in proposed PBPK models treat the rate of elimination of TCDD in either of two ways (Emond *et al.*, 2006). The models described by Wang *et al.* (2000), Maruyama *et al.* (2002), and Emond *et al.* (2004) assume a constant hepatic clearance rate for TCDD.

Andersen *et al.* (1997), Emond *et al.* (2005) and Kohn *et al.* (1996) assume a dose dependent rate of hepatic elimination of TCDD that increases with dose. In the toxicokinetic model of van der Molen *et al.* (1998; 2000) the t½ of TCDD is varied by body composition, but not dose. Aylward *et al.* (2005a) extended the Carrier *et al.* (1995a, b) model by incorporating elimination due to lipid partitioning of TCDD from the blood into the large intestine based on published human data (Moser and McLachlan, 2002). In the Carrier model (Carrier *et al.,* 1995a,b), hepatic concentrations increase with dose in a non-linear manner due to hepatic sequestration.

As the fraction of TCDD in the liver increases from 15 to 70%, there is a 5-fold maximum induction of the elimination rate in rats. For humans, the model estimated that the fraction of TCDD in the liver ranged from 1 to 70%, resulting in approximately a 70-fold induction of TCDD elimination at high exposures (Carrier *et al.,* 1995a,b; Emond *et al*., 2006).

Despite these mechanistic differences, most models provide reasonable fits to the experimental data. Dioxins are highly lipophilic, and concentrate in adipose tissue. Recent studies suggest that body fat mass influences the elimination of TCDD (van der Molen *et al.,* 1998; 2000). Michalek and Tripathi (1999) found that the TCDD t½ increases with body mass index (BMI) in humans. Increasing BMI alters the pharmacokinetics of lipophilic chemicals. The consequence of increased distribution of lipophilic compounds into the adipose compartment is the alteration of concentration of xenobiotic metabolizing enzymes (Emond *et al.*, 2006).

Emond *et al.* (2006) have recently described a PBPK model that is optimized for the induction of CYP1A2 that occurs at elevated exposures (doses) of TCDD.. The model assumes a maximum forty-fold induction of CYP1A2 resulting in estimates of the inducible elimination rate ($hour^{-1}$) that range from 0.06 hr^{-1} for 10^{-3} µg/kg to 2.46 hr^{-1} at exposures up to 10^{3} µg/kg. This results in terminal elimination t½ estimates that range from approximately 75 days to approximately ten days at the higher exposures (Emond *et al.*, 2006).

This use of a variable elimination rate that corresponds to enzyme induction and receptor binding provides better fits to the experimental data of Santostefano *et al.* (1998) when compared to models that use a fixed rate of elimination (Emond *et al.*, 2006). At conditions of maximal induction (10 µg/kg) Emond *et al.* (2006) reported that the inclusion of the CYP1A2 hepatic sequestration of TCDD in the liver in the PBPK model resulted in higher TCDD concentrations in the blood, and a good fit with experimental observations. On the other hand, removal of the CYP1A2 sequestration decreased the concentration of TCDD in the blood and an underestimate of overall elimination rate (compared to observed values) by over an order of magnitude (Emond *et al.*, 2006).

6.2.4 Toxicological Reference Values

Several regulatory agencies have derived TRVs for dioxins. The following section provides a review of those most relevant to the current assessment. Where available, TRVs derived by Health Canada have been selected for the purpose of this assessment.

The U.S. EPA draft dioxin assessment derived a cancer slope or potency factor based on occupationally exposed cohorts of workers (U.S. EPA, 2003). The U.S. EPA used a traditional default linear extrapolation tool that by design does not have the ability to find or estimate the presence of a threshold (Popp *et al.*, 2006). The U.K. Committee on Carcinogenicity reviewed the U.S. EPA approach (U.K COC, 2001) and concluded that modeling of dose-response data from the industrial cohort epidemiology studies was limited by the variable quality of the exposure estimates and the uncertainties associated with back-extrapolating estimates of body burden. The Committee considered the linear extrapolation to estimate risks at background body burdens to be unacceptable. The COC found that the predicted kinetic profile of the elimination of TCDD and other dioxins following occupational exposure (predominantly *via* the skin) over several decades was considerably different to that of the general population whose exposure occurred primarily *via* the diet (U.K COC, 2001). They concluded that the review of cancer epidemiology studies and risk characterization of cancer undertaken by U.S. EPA was a detailed

and valuable scientific assessment, but that the derivation of ED_{01} (ED_{01}- the exposure dose responsible for 1% excess in the lifetime risk of cancer), cancer slope factor and risk at background exposure levels were not.

Based on available evidence from human, animal and mechanistic studies, most regulatory agencies consider dioxin a threshold carcinogen; *i.e.*, it is believed there is a level of exposure below which cancer risk is not or is negligibly increased above background incidence (WHO, 2000a; JECFA, 2001; ECSCF, 2001). Popp *et al.* (2006) concluded from their weight-of-evidence analysis that based on all considerations, a non-linear, threshold dose-response relationship is best scientifically supported to estimate human cancer risk from TCDD exposures. They note that the observed threshold in rats lies somewhere between 22 and 28 ng/kg (5 days/week) nominal dose rate. Although proof of a threshold can never be absolute, the level of certainty in the case of dioxin is high because of the concordance of many lines of evidence (Popp *et al.*, 2006).

With the exception of the U.S. EPA, who have proposed cancer potency factors derived from occupational studies by which low dose cancer risks can be predicted (U.S. EPA, 2003), regulatory agencies have proposed or established tolerable daily or weekly intakes for dioxin based on animal data rather than human data. Reasons cited include: a) most available epidemiological studies do not reflect the most sensitive population identified by animal studies (*i.e.*, exposure during development, particularly *in utero*); b) the considerable uncertainty in exposure assessments and inadequate allowance for confounding factors; and, c) patterns of exposure which do not reflect exposures in the general population, which are mainly from the diet (U.K COT, 2001). The Scientific Committee on Food in Europe noted that a number of effects including cancer, produced in occupational or accidentally exposed humans are clearly high dose effects (ECSCF, 2001).

Until recently the recommended a tolerable intake level for dioxin based on two key chronic (*i.e.*, long-term) studies in rats. One study was a multi-generation reproductive study that identified reductions in fertility in the second generation of rats exposed to 10 ng TCDD/kg body weight per day (Murray *et al.*, 1979). The other study was a 2-year carcinogenicity bioassay that identified elevated tumour rates at doses of 10 ng/kg body weight and above (Kociba *et al.*, 1978). In both studies a no observable adverse effects level (NOAEL of 1 ng/kg bw/day was identified. Health Canada applied an uncertainty factor of 100 to this NOAEL to account for potential interspecies and intraspecies variability, resulting in a TDI of 10 pg TEQ/kg bw/day. This was considered to be protective for both adverse effects on reproduction and development as well as cancer (Feeley and Grant, 1993). This remains the "official" Canadian TDI for dioxin to this date. Several other countries or agencies have or had recommended the same TDI, including the WHO (1991), the U.K., the Netherlands and the Nordic Group.

More recently, reevaluations of the health risks posed by dioxin-like compounds have been undertaken by the WHO (1998; 2000a) and other regulatory bodies (*e.g.*, the European Commission Scientific Committee on Food and the U.K. Committee on Toxicity in Chemicals in Food) as well as the U.S. EPA (2003). The U.S. EPA approach and conclusions with respect to safe levels are described below but some key characteristics of the WHO and related evaluations have been summarized as follows:

- Body burdens were used as dose metrics rather than daily doses. This permitted comparison across species that exhibit very different rates of metabolism and excretion for dioxin-like compounds. Half-lives for 2,3,7,8-TCDD across species range from 20 to 30 days in rats, to approximately 400 days in monkeys and between 5 and 11 years in adult humans. Thus, rodents require considerably higher doses (100 to 200-fold) to reach the same equivalent body burdens at steady state as humans do and humans have a much higher potential for accumulation of TCDD.

- The evaluation deviated from the earlier evaluations of TCDD by not using the long-term rat studies to identify critical endpoints for the derivation of the TDI. The majority of the studies identifying the most sensitive responses in the recent evaluations involved acute gavage (bolus) exposure at a critical time during pregnancy.

- Although studies in humans were carefully evaluated, the evaluation was ultimately based on sensitive endpoints in experimental animals; and,

- Developmental, reproductive and hormonal effects following 2,3,7,8-TCDD exposure of female rats and monkeys were identified as the most sensitive adverse effects reported; *i.e*., the adverse effects occurring at the lowest body burdens (ECSCF, 2001).

As noted by Aylward *et al.* (2005a), all of the recent assessments focus on a body of data that indicates that the most sensitive responses to TCDD in experimental animals appear to be effects on the development of offspring following *in utero* exposure to TCDD, in particular alterations in male rat reproductive parameters. The WHO consultation recommended a TDI of 1 to 4 pg TEQ/kg based on body burdens in experimental animals associated with developmental and reproductive effects in rats and monkeys (WHO, 1998; 2000b). A range of reported animal lowest observed adverse effect levels (LOAELs) that occurred at body burdens measured in the range of 10 to 73 ng/kg. Using pharmacokinetic calculations, these body burdens were transformed into estimated daily human intakes that corresponded to similar body burdens in humans under steady state conditions (WHO, 2000b).

Although there were some differences in assumptions and calculations, ECSCF (2001), JECFA (2001), and the U.K. COT (2001) recommended a similar tolerable intake based on Faqi *et al.* (1998). The provisional tolerable monthly intake of 70 pg TEQ/kg represents the mid-range of TDI estimates (JECFA, 2001). Health Canada participated in this evaluation and they have provisionally adopted this TDI for risk assessment purposes but they are in the midst of a comprehensive reassessment of the risks posed by dioxins (Health Canada, 2005). Assuming 20 days per month, Health Canada (2005) has endorsed 2.3 pg TEQ/kg bw/day as the tolerable level (70 pg TEQ/kg bw/month ÷ 30 days/month). The U.K. Committee on Toxicity in Food (U.K COT, 2001) derived a TDI of 2 pg TEQ/kg bw/day (Faqi *et al.*, 1998).

Table 6-1 presents a summary of the recent tolerable intake levels recommended by various agencies.

Table 6-1 Tolerable Daily Intakes Established by Regulatory Agencies or Scientific Bodies After Recent Rre-evaluations of Dioxin and Dioxin-like Compounds

Regulatory agency/scientific body	Tolerable intake
ATSDR (1998)	Chronic MRL= 1 pg TEQ/kg bw/day Intermediate MRL = 20 pg TEQ/kg bw/day Acute MRL = 200 pg TEQ/kg bw/day
Health Canada (2004b; 2005)	Official TDI= 10 pg TEQ/kg bw/day Provisional TDI = 2.3 pg TEQ/kg bw/day
World Health Organization (WHO, 2000a)	Tolerable daily intake = 1-4 pg TEQ/kg bw/day
European Commission (ECSCF, 2001)	Tolerable weekly intake: 14 pg TEQ/kg bw/wk (equivalent to 2 pg TEQ/kg bw/day)
United Kingdom (COT, 2001)	Tolerable daily intake: 2 pg TEQ/kg bw/day
Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2001)	Provisional tolerable monthly intake: 70 pg TEQ/kg bw/ month (equivalent to 2.3 pg TEQ/kg bw/day)
U.S. EPA (2003; 2004)	Risk-specific dose (RsD) = 0.01 – 0.1 pg TEQ/kg bw/day for incremental cancer risks of 1 in a million or 1 in 100,000, respectively.
	0.13 pg TEQ/kg bw/day. Margin of exposure (MOE) approach: <0.1 pg TEQ/kg bw/day relative to background intake

In the Priority Substance List assessment, Health Canada concluded that there is no adequate demonstration that human populations exposed to dioxins and furans have suffered excess cancer. However, based on the results of studies in animals, it was assumed that chlorinated dioxins and furans are non-genotoxic carcinogens and reproductive toxicants with a threshold, and therefore a tolerable daily intake for human exposure was derived (CEPA, 1990). Based on JECFA (2001); Health Canada (2004b; 2005) has most recently adopted a tolerable level of 70 picograms per kilogram body weight per month or approximately 2.3 picograms per kilogram of body weight per day. The Health Canada tolerable daily intake or TRV of 2.3 pg TEQ/kg body weight/day has been adopted for the current assessment.

ATSDR (1998) has derived an acute MRL of 200 pg/kg bw/day based on immunological effects in female mice (Burleson *et al*., 1996). ATSDR (1998) classified this as a "less serious" effect. "Serious" effects were reported by Mably *et al*. (1992) at a dose of 0.064 μg/kg body weight.

6.2.5 Body Burden of Dioxin

Dioxins, like many chemicals, accumulate in various body tissues through a variety of exposure routes (inhalation, ingestion, or dermal). A common approach for evaluating chemical loading and associated effects in humans is a body burden approach. The term "body burden" refers to the concentration of chemical in the body at a specific point in time. It accounts for differences in toxicokinetics and may account for sensitivity differences between species.

A half-life of 7.1 years has been assumed for this study, as it represents a conservative mid-point of TCDD specific half-lives noted in the literature, and is consistent with those reported by Pirkle *et al*. (1989), Wolfe *et al*. (1988) and Aylward *et al.* (2005). There exist a range of half-lives reported in the literature of up to 11.3 years. Essentially all exposures for herbicides that contained 2,4,5-T (Agents Orange and Purple as well as other formulations that were prepared for some plots) were exclusively to TCDD as virtually no significant levels of other dioxin congeners were present. The response to acute exposure to TCDD in humans is sequestration in

the liver and an initial phase of rapid elimination; this suggests that the assumption of a constant half-life for large exposures to TCDD is overly conservative. The constant half-life is utilized since current exposure and risk estimation methods do not accommodate a variable elimination rate.

As outlined in Table 6-2, it is possible to relate doses at which effects occur to body burdens within test species. In a similar manner, the Health Canada (2004b) TRV of 2.3 pg TEQ/kg body weight per day can be expressed on the basis of a body burden. Using a simple pharmacokinetic model provided by the U.S. EPA Dioxin Reassessment Manual (U.S. EPA, 2003), as discussed in Section 7.1, and the assumption that the TRV represents a lifetime average dose, the Health Canada (2004b) TRV can be expressed as a body burden of 27.8 pg TEQ/g lipid. This value is referred to as the Body Burden$_{TRV}$ or BB_{TRV}.

Table 6-2 LOAELs Identified by WHO (2000a) With Measured or Derived Body Burdens

Study	Response (LOAELs)	Dose Given (pg TEQ/kg bw)	Body Burden (pg TEQ/g lipid)
Rats			
Gray *et al.*, (1997a) Mably *et al.*, 1992)	Decreased sperm counts in offspring	64,000	28
Gehrs *et al.*, (1997) Gehrs and Smailowicz (1998)	Immune suppression in offspring	100,000	50
Gray *et al.*, (1997b)	Increased genital malformations in offspring	200,000	73
Monkeys			
Schantz and Bowman (1989)	Neurobehavioral (object learning) effects in offspring	160	42
Rier *et al.*, (1993)	Endometriosis	160	69

Adapted from WHO (2000a)

Similarly, ATSDR (1998) has provided body burdens corresponding to the MRLs, LOAELs and NOAELs that they have reviewed. These are provided in Table 6-3.

Table 6-3 Estimated Body Burdens of TCDD that Correspond to MRLs (from ATSDR, 1998)

Duration	Risk or effect level	Exposure (pg TEQ/kg bw/day)	Body Burden (pg TEQ/g lipid)
Acute	MRL	200	0.16
	NOAEL	5,000	4
	LOAEL	10,000	8
Intermediate	MRL	20	0.66
	NOAEL	700	23
	LOAEL	5,000	164
Chronic	MRL	1	0.26 (peak maternal) 0.76 (offspring at weaning)
	LOAEL	120	32 (peak maternal) 68 (offspring at weaning)

The human health effects of dioxins in humans include dermal toxicity, immunotoxicity, reproductive effects and teratogenicity, endocrine disruption and carcinogenicity (WHO, 2000a). Epidemiological studies of dioxin exposed workers have not found effects beyond prolonged chloracne (CEPA, 1990). Table 6-4 outlines the health effects in humans associated with estimated 2,3,7,8-TCDD body burdens following exposure at various durations.

Table 6-4 Health Effects in Humans Associated with Estimated 2,3,7,8-TCDD Body Burdens following Exposure (Adapted from ATSDR, 1998)

Exposure Duration (days)	Effect	Current Serum levels (pg TEQ/g lipid)		Estimated levels at the time of exposure termination		Elimination half-life (years)	Reference
		Mean	Range	Serum level (pg TEQ/g lipid)	Body Burden (ng/kg)		
<1	Chloracne in Children	19411	828-56,000	NA	2876	NA	Mocarelli *et al.*, 1991
<1	No increased risk of spontaneous abortion	NR	>10	>110	>24	7.1	Wolfe *et al.*, 1995
NR	Chloracne in 5/7 subjects	185	36-291	1900	493	NR	Schecter *et al.*,1994
11	Chloracne	604	163-1935	2935	646	7	Jansing and Korff, 1994
6.5	Immunosuppression	330	43-874	942-1108	207-244	8.5	Tonn *et al.*, 1996
<1	Change in sex ratio of children	540-mother 791-father	126-1650 104-2340	NA	119 174	NA	Mocarelli *et al.*, 1996
≥ 1	Increased cancer mortality rate	418	NR	1408-8444	310-1858	8.5	Fingerhut *et al.*, 1991

NR – Not Reported; NA – Not Applicable

Collins *et al.* (2006) evaluated the serum levels of PCDD/PCDFs in chlorophenol workers at the Midland, Michigan Dow Chemical plant. Persons working at this plant would have been exposed to dioxins and dibenzofurans as unintended by-products generated in trichlorophenol and PCP production. Examination of medical records indicated that approximately 15% of the 2072 workers were diagnosed with definite or probable chloracne (Collins *et al.*, 2006). Table 6-5 outlines the levels of dioxins in different exposure groups.

Table 6-5 Arithmetic Mean of Lipid-adjusted Serum Dioxin Level by Exposure Group in Parts Per Trillion (ppt)

Exposure Group		2,3,7,8-TCDD mean (pg TEQ/g; ppt)	TEQ-WHO for PCDD/PCDF mean (pg TEQ/g; ppt)
Chlorophenol exposed workers	Chloracne (TCP) n=17	30.5*	86.8*
	Chloracne (PCP) n = 18	9.9	68.4*
	Chlorophenol department, no chloracne n = 17	7.9	40.3
	Tradesmen with plant-wide duties n = 10	20.7	85.0*
All exposed workers n= 62		16.7*	68.4*
Comparison group n = 36		6.0	32.7

*Significantly different than comparison group
TCP - trichlorophenol
PCP - pentachlorophenol
Adapted from Collins *et al.* (2006)

The human evidence clearly indicates that chloracne is the most consistent adverse effect associated with exposure to TCDD. Chloracne was diagnosed in at least 193 (0.6%) Seveso residents, mostly children, exposed during the accident (Greene *et al*., 2003). Among other populations with known exposure to TCDD, US Air Force personnel in Vietnam were not reported to have developed chloracne (WHO, 2000).

Serum levels of TCDD and Hexachloro-CDD have been measured in chloracne cases of Seveso residents (Mocarelli *et al.*, 1991) and German (BASF) chemical workers (Ott *et al.*, 1993; Jung *et al.*, 1994). Mocarelli *et al.* (1991) described chloracne in people from Zone A in Seveso who had serum TCDD levels ranging from 828 to 56,000 pg/g, lipid adjusted. With the exception of 1 person who developed less severe chloracne, all people who had TCDD levels over 12,000 pg/g (ppt), lipid adjusted, developed severe chloracne. Several people with levels below 12,000 ppt developed less severe chloracne; the lowest reported TCDD level associated with chloracne was 828 ppt at the time of the accident. In the group that developed chloracne, >95% were under 20 year old, including the person with a serum lipid TCDD concentration of 828 ppt. Children appear to develop chloracne at lower serum TCDD concentrations than adults (Mocarelli *et al.*, 1991; Greene *et al.*, 2003).

A conservative approach that assumed the lowest level associated with chloracne in children identified an appropriate choice of a LOAEL for TCDD exposure should be based on chloracne in children (Greene *et al.*, 2003). On this basis, it was suggested that a safe human serum lipid adjusted level (or NOAEL) would be approximately 80 pg/g (Greene *et al.*, 2003).

Chloracne is normally thought of as an acute endpoint; that is, the current body burden causes an effect that lessens or disappears when the person is removed from the source of exposure, and thus is best measured using peak serum concentrations (Greene *et al.*, 2003).

Dioxins and dioxin-like chemical patterns in blood and other tissues provide a signature of their source (Schecter *et al.,* 2006). Schecter (*et al.,* 2006) compared human tissue levels and toxic equivalents of dioxins and dibenzofurans from different exposures. Table 6-6 provides patterns of patients exposed to different levels of dioxins. As a comparison or background value, Schecter *et al.* (2006) provides a value of 3.6 ppt and 6.4 ppt for the general populations of the U.S. and

Japan of 2,3,7,8-TCDD. Total TEQ "background" values are 22.8 and 24.6 ppt. No sample size for the USA or Japanese population was reported in Schecter *et al.* (2006).

Table 6-6 Comparison of Human Tissue Levels and Toxic Equivalents of Dioxins and Dibenzofurans from Different Exposures[a]

	Fat (USA) level (pg TEQ/g or ppt, lipid)		Blood (Japan) (pg TEQ/g)	
Dioxin	**General Population[b]**	**Pentachlorophenol-exposed person[c]**	**General Population[d]**	**Incinerator worker[d]**
2,3,7,8- Tetra-CDD*	3.6	33	2.6	6.4
Total TEQ	22.8	609	24.6	1467

[a] Adapted from Schecter *et al.*, 2006
[b] From Schecter *et al.*, 1990
[c] From Ryan *et al.* 1987
[d] From Schecter *et al.*, 2001

In the *Third National Report on Human Exposure to Environmental Chemicals* the Center for Disease Control (CDC, 2005) published data for the background levels for sampling conducted in 1999 to 2000 and 2001 to 2002. For TCDD levels in a sub-sample of the 95th percentile in women and non-hispanic blacks (20 years and older), CDC (2005) reports values of 6.4 (n=669) and 7.4 pg TEQ/g (n=217) of lipid respectively, and 50.7 and 52.1 pg TEQ/g of whole weight. The remaining sub-sampled groups were below the limit of detection (LOD= 5.8 pg TEQ/g lipid). Although CDC (2005) does not report TEQ background levels this information is valuable in that it offers a reference for the current background levels in industrialized countries.

In summary, it is evident from the available data in Schecter *et al.* (1994), Schecter *et al.* (2006), Collins *et al.* (2006) and as a comparison CDC (2005), that values in the range of 22.8 to 32.7 ppt TEQ Dioxins in lipid and a range of 3.6 to 6.0 ppt 2,3,7,8-TCDD in lipid are representative of the background population in industrialized countries. As discussed in Lorber (2002), dioxin analysis of carbon-dated sediment cores of lakes and rivers, preserved meat samples and limited body burden measurements of dioxin-like chemicals indicates that exposure of Americans to dioxin-like compounds increased during the 1940s and 1950s, reached a peak in the 1960s and 1970s and decreased to lower levels in the 1980s and 1990s. Body burdens are predicted to follow a similar trend. This is further discussed in Appendix C.

6.3 Epidemiological Evidence of Agent Orange/Purple Exposure

The following provides a brief summary of conclusions of the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides (IOM, 2005).

Several different types of herbicide were used by U.S. forces in Vietnam; these were identified by code names referring to the color of the band around the 55-gallon drum that contained the chemical. These included Agents Orange, White, Blue, Purple, Pink, and Green. From 1962 to 1965, small quantities of Agents Purple, Blue, Pink, and Green were used. From 1965 to 1970, Agents Orange, White, and Blue were employed; from 1970 to 1971, only Agents White and Blue were used in the defoliation program (Young and Reggiani, 1988) (Table 6-7).

Table 6-7 Major Herbicides Used in Operation Ranch Hand in Vietnam (1967-69)

Herbicide Code Name	Formulation	Purpose	TCDD	Period of use
PURPLE	2,4-D; 2,4,5-T	defoliation	45 ppm	1962-1964
BLUE (Phytar 560-G)	Cacodylic acid	grasses, rice		1962-1971
PINK	2,4,5-T	defoliation	?	1962-1964
GREEN	2,4,5-T	crop destruction	?	1962-1964
ORANGE, ORANGE II	2,4-D, 2,4,5-T	defoliation	2 ppm	1965-1970
WHITE	2,4-D; picloram	defoliation, long-term		1965-1971

Adapted from NAS report on Vietnam Veterans and AO (IOM, 2005)

Approximately 1.5 million U.S. military personnel served in Vietnam during the period of heaviest herbicide spraying, 1967 to 1969 (Frumkin, 2003; IOM, 2005). Most of the large-scale spraying operations in Operation Ranch Hand were conducted using airplanes and helicopters. Ranch Hand personnel who loaded airplanes and helicopters probably sustained some of the heaviest exposures (Frumkin, 2003). Exposures have been assumed to have occurred primarily through inhalation, ingestion, and skin absorption, but also possibly through more unusual routes such as through skin lesions and ocular absorption (Frumkin, 2003). Most health issues related to herbicide use in Vietnam revolve around the use of Agent Orange (AO).

Epidemiologic studies of Vietnam veterans have the greatest potential for providing direct evidence of possible the health effects of Agent Orange exposure. Despite the large number of soldiers in theater, the number who received documented or high levels of exposure to the herbicide were relatively few. Thus the population from which to extract cancer statistics is small, and therefore the power of any epidemiological analysis is always brought into question.

The Vietnam Experience Study (VES) conducted by the CDC was a historical cohort study that compared 9,324 Vietnam Army veterans with 8,989 Vietnam era Army veterans who served elsewhere. It included a mortality study; health interviews; and clinical, psychological, and laboratory evaluation of a random sample of veterans who completed the health interview. The total number of cancer deaths in the VES was inadequate to yield information on specific cancer types.

The U.S. Department of Veterans Affairs has also conducted a number of epidemiological studies that have addressed specific exposure groups, case-control studies and large-scale cohort studies. Additional studies have been carried out with veterans from various of the States in the U.S. and by the Government of Australia. These studies also have suffered from inadequate numbers, poor exposure assessment and other factors that limit their predictive power.

A study initiated by the U.S. Air Force: The Air Force Health Study focused exclusively on 1,200 Ranch Hand veterans along with 1,300 comparison veterans who had not participated in the program. Although this study was directed at Agent Orange exposure, the relatively small number of subjects included in this twenty year prospective study and the even smaller numbers who were characterized as having elevated levels of TCDD greatly limited the statistical power to detect increases in cancer incidence (Frumkin, 2003).

An important source of information that relates to how to assess the toxic potential of human exposure to TCDD may be found in occupational cohorts and among people who have experienced industrial accidents in Germany or Seveso, Italy. Each of these populations differs from the Vietnam veterans and from those in the Canadian Military in demographic composition,

the nature of the dioxin exposures, and other factors such as diet and concomitant chemical exposures. These should also be regarded as sources of bias or confounding.

6.3.1 Carcinogenic Effects Associated with Agent Orange/Purple

Soft Tissue Sarcoma

Studies of Vietnam veterans have not demonstrated an increase in the level of soft tissue sarcoma (IOM, 2005). In particular, no association with soft tissue sarcoma has been seen in the Ranch Hand study, in another study of 10,716 marines who served in Vietnam, a large case-control study of sarcoma patients in VA hospitals, the Selected Cancers Study, or studies of veterans in Michigan, Massachusetts, or other states.

Phenoxy herbicide exposure has been linked with increased incidence of soft tissue sarcomas by a series of case-control studies in Sweden and by cohort and case-control studies of industrially exposed workers. Many studies of farmers and agricultural workers show an increase in soft tissue sarcomas, which may relate to herbicide exposure.

Non-Hodgkin Lymphoma

Most studies of Vietnam veterans have not demonstrated an increase in non-Hodgkin lymphoma (NHL). The Selected Cancers Study showed that Vietnam service was associated with a 50% increased risk of NHL, but self-reported Agent Orange exposure was not associated with increased risk. Similarly, in the CDC's Vietnam Experience Study, there were seven NHL deaths among the 8,170 Vietnam veterans and only one NHL death among the 7,564 non-Vietnam veterans.

Based on military job titles, there was no suggestion that the seven Vietnam veterans with NHL had sustained Agent Orange exposure. By contrast, the Ranch Hand study showed no increase in NHL, nor did the VA mortality study of 33,833 Army and Marine Vietnam veterans, a case-control study of 201 Vietnam veterans with NHL, or numerous state-level studies.

Several case-control studies have found an association between phenoxy herbicide exposure (usually on the job) and NHL. Numerous other studies of farmers and agricultural workers also suggest this association, although cohort studies of herbicide production workers have generally been negative or report non-significant associations because of a very small numbers of cases. Dioxin exposure was not associated with NHL in either the NIOSH occupational study or the Seveso follow-up.

Hodgkin Disease

Studies of Vietnam veterans have not demonstrated an increase in Hodgkin disease. In particular, the Ranch Hand study did not show an increase in these tumours, nor did a study of 33,833 Army and Marine Vietnam veterans, the Selected Cancers Study, a case-control study of 283 Vietnam-era veterans with Hodgkin disease, or studies of veterans in Michigan, New York, or other states.

Non-military studies that have tried to associate phenoxyherbicide exposure to increased incidence of Hodgkin disease have given mixed results. Hodgkin disease was linked to phenoxy herbicide and chlorophenol exposure in one case-control study in Sweden, and another study that failed to reach statistical significance. The large occupational study of 5,132 chemical manufacturing workers in the United States did not show an increase in Hodgkin disease. The Seveso follow-up showed no cases of Hodgkin disease in the zone of greatest dioxin exposure, and a small excess of cases in the other zones. Farmers and agricultural workers show an increase in Hodgkin disease which has been associated with phenoxy herbicide exposure.

Chronic Lymphocytic Leukemia (CLL)

An analysis of the results from epidemiologic studies specifically concerning CLL revealed that the majority of studies of herbicide exposure support the hypothesis that such exposure can contribute to the development of NHL. There is also evidence (from the general scientific literature but not from veterans exposed to AO) that exposure to the herbicides 2,4-D and 2,4,5-T appears to be associated with the occurrence of CLL (IOM, 2005). The only new study of leukemia since 2002 was an update of cancer incidence among the Ranch Hand veterans compared to a cohort of other Air Force veterans (Akhtar *et al*., 2004). The small number of cases did not permit analysis by separate types of leukemia, but there was no basis to reverse the conclusions of the last update.

Respiratory Cancers

Studies of Vietnam veterans have not shown a consistent pattern of increases in respiratory cancers (lung, trachea/bronchus, larynx). The Veterans Affairs studies did not reveal increased mortality from these cancers in Vietnam veterans, nor did the study of Army Chemical Corps veterans. The Ranch Hand study suggested an increase in lung cancer, with a relative risk of 3.7, but this finding was based on only 10 deaths. A high prevalence of smoking in the Ranch Hand population may have accounted for this finding. Most studies of workers with occupational herbicide exposure, such as herbicide manufacturing workers, herbicide applicators, farmers, and forest and soil conservationists have shown no excess of lung cancer. Similarly, follow-up of the Seveso accident has not shown an association between dioxin exposure and lung cancer. During a follow-up of an industrial accident in Germany an increase in respiratory cancers was reported, but this was based on small numbers of cases.

Prostate Cancer

The Ranch Hand studies showed an excess of prostate cancer in Ranch Hand veterans with elevated dioxin levels who served prior to 1969 (Pavuk *et al*., 2006).

With some exceptions most studies of workers occupationally exposed to phenoxyacetic acid herbicides do not show an excess of prostate cancer.

Follow-up of the Seveso accident revealed a non-significant 20% excess of prostate cancer, as did the NIOSH study of chronic dioxin exposure. On the other hand, follow-up of other acute dioxin exposure incidents has showed no excess of prostate cancer.

Multiple Myeloma

None of the studies of Vietnam veterans are informative regarding multiple myeloma risk, because the numbers of cases have been consistently small. Overall the evidence linking Agent Orange to multiple myeloma is sparse and indirect.

Other studies of people exposed to pesticides, herbicides, and/or dioxins have been suggestive of an association. Several studies of farmers and agricultural workers have reported a small increase in multiple myeloma, although other studies show no excess of this neoplasm. Follow-up of the Seveso accident shows a deficit of multiple myeloma among exposed males but an excess among females (relative risk 3.7 based on four cases), a disparity that remains unexplained. Similarly, the NIOSH study of 5,132 workers exposed to dioxins showed a marginally significant doubling of multiple myeloma risk, based on 10 cases.

Acute Myelogenous Leukemia in the Children of Veterans

Three studies have pointed to an association between paternal Agent Orange exposure and acute myeloid leukemia (AML) in children. The first was a case-control study of 204 children with AML, reported by the Children's Cancer Study Group, a U.S.-Canada consortium. The odds ratio associated with paternal long-term occupational pesticide exposure was 2.7 (95% CI, 1.0– to 7.0). As for maternal exposure, seven case mothers and no control mothers reported such exposure. The risk was elevated for children diagnosed before the age of six and for children who had sustained direct pesticide exposure. "Pesticides" in this study included both insecticides and herbicides, so it is not clear which agents were associated with the increased risk.

The second study was a survey of nearly 50,000 Australian Vietnam veterans. This study also found an increase in AML among the children of Vietnam veterans, with a relative risk of 4.3. The risk of acute lymphocytic leukemia (ALL) was not increased in this study.

The third study, a case-control study of 1,805 cases of ALL and 528 cases of AML, was also reported from the Children's Cancer Group. Although military service in general conferred no increased risk of childhood leukemia, service in Vietnam or Cambodia was associated with an odds ratio of 1.7 for AML (and no increased risk of ALL). Self-reported exposure to Agent Orange was not associated with increased risk.

Other Cancers

The IOM (2005) has concluded that there is inadequate or insufficient evidence to determine whether an association exists between exposure to Agent Orange and the following cancers:

- Hepatobiliary cancers;
- Nasal/nasopharyngeal cancer;
- Bone cancer;
- Breast Cancer;
- Urinary bladder cancer;
- Renal cancer;
- Testicular cancer;
- Female reproductive cancer (cervix, uterus, ovary);
- Leukemia (other than CLL); and,
- Skin cancers.

Gastrointestinal (GI) Cancer

Cancers of the esophagus, stomach, pancreas, colon, and rectum have been extensively studied in Vietnam veterans, occupational groups with herbicide exposure, and people exposed to dioxins. Generally these studies have failed to demonstrate evidence of an association between these exposures to Agent Orange or phenoxy herbicides and any GI cancer.

Brain Cancer

There has been no connection to confirm an association between service in Vietnam, occupational herbicide exposure, or dioxin exposure, and brain cancer

6.3.2 Evidence of Health Effects Associated with Herbicide Exposure

Sufficient Evidence of an Association

Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between herbicides and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence of an association. There is sufficient evidence of an association between exposure to herbicides and the following health outcomes (IOM, 2005; Schecter *et al.*, 2006):

- Chronic lymphocytic leukemia (CLL);
- Soft-tissue sarcoma;
- Non-Hodgkin's lymphoma;
- Hodgkin's disease; and,
- Chloracne.

Limited or Suggestive Evidence of an Association

Evidence is suggestive of an association between herbicides and the outcome but is limited because chance, bias, and confounding could not be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent. There is limited or suggestive evidence of an association between exposure to herbicides and the following health outcomes:

- Respiratory cancer (lung and bronchus, larynx, and trachea);
- Prostate cancer;
- Multiple myeloma;
- Early-onset transient peripheral neuropathy;
- Porphyria cutanea tarda;
- Type 2 diabetes (mellitus); and,
- Spina bifida in offspring of exposed individuals.

Inadequate or Insufficient Evidence to Determine Whether an Association Exists

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency. There is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and the following health outcomes:

- Hepatobiliary cancer;
- Oral, nasal, and pharyngeal cancer;
- Bone and joint cancer;
- Skin cancers (melanoma, basal cell, and squamous cell);
- Breast cancer;
- Female reproductive cancer (cervix, uterus, ovary);
- Testicular cancer;
- Urinary bladder cancer;
- Renal cancer;
- Leukemia (other than CLL);
- Abnormal sperm characteristics and infertility;
- Spontaneous abortion;
- Neonatal or infant death and stillbirth in offspring of exposed individuals;
- Low birth-weight in offspring of exposed individuals;
- Birth defects (other than spina bifida) in offspring of exposed individuals;
- Childhood cancer (including acute myelogenous leukemia) in offspring of exposed individuals;
- Neurobehavioral disorders (cognitive and neuropsychiatric);
- Movement disorders, including Parkinson's disease and amyotrophic lateral sclerosis (ALS);
- Chronic peripheral nervous system disorders;
- Respiratory disorders;
- Gastrointestinal, metabolic, and digestive disorders (changes in liver enzymes, lipid abnormalities, ulcers);
- Immune system disorders (immune suppression, autoimmunity);
- Circulatory disorders;
- AL amyloidosis;
- Endometriosis; and,
- Effects on thyroid homeostasis.

Limited or Suggestive Evidence of *No* Association

Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter, are consistent in not showing a positive association between any magnitude of exposure to herbicides and the outcome. A conclusion of "no association" is inevitably limited to the conditions, exposure, and length of observation covered by the available studies. *In addition, the possibility of a very small increase in risk at the exposure studied can never be excluded.* There is limited or suggestive evidence of *no* association between exposure to herbicides and the following health outcomes:

- Gastrointestinal tumors (esophagus, stomach, pancreas, colon, rectum); and,
- Brain tumors.

6.3.3 Dioxin Body Burdens in Vietnam Veterans

A study reported by Kang *et al.* (2001) found 2,872 members of the Army Chemical Corps served in Vietnam between 1966 and 1971. These were matched with another group of 2,737 individuals who served during approximately the same period but were never in Vietnam. From these matched groups 284 Vietnam veterans and 281 non-Vietnam veterans were randomly selected for a self reported interview of exposure (Kang *et al.*, 2001). Fifty members from each group were selected as blood donors to characterize levels of dioxins in their blood in 1999 (approximately 20 to 30 years after the exposure period. Blood analyses were carried out by the CDC. Ninety-five (95) of the one hundred samples of blood from volunteers met all the criteria for analyses required by the CDC (Kang *et al.*, 2001).

Out of the 95 for whom dioxins (TCDD + six additional PCDDs) had been determined, 31 recorded values for TCDD below the detection limit (<LOD). For each of these values a concentration equivalent to one half the mean detection limit was substituted.

The first question addressed was whether there were notable differences among exposed veterans from the Army Chemical Corps who served in Vietnam for levels of TCDD in blood (lipid adjusted values) but had different levels of exposure to herbicides (*e.g.*, non-sprayers *vs.* sprayers).

The geometric mean of values for levels of TCDD in the blood of Corps veterans who used AO or other herbicides produced a lognormal distribution. Blood values used for calculating meam exposure concentrations were the natural logarithm of the determined value in ppt adjusted for lipid concentration (Kang *et al.*, 2001). From the table presented below (Table 6-8) it can be seen that the only significant difference between veterans who handled herbicides and those who never did was the lipid adjusted concentration of TCDD in blood.

Table 6-8 Comparison of Lipid-adjusted Concentrations (ln [TCDD] ppt) of the Seven Analytes in Vietnam Veterans Who Sprayed AO and the Other Herbicides With Veterans Who Never Sprayed.[a]

Dioxin	Herbicide Sprayer Population[b]	Non-sprayer population	P value[c]
2,3,7,8- Tetra-CDD*	1.33± 0.20	0.86± 0.14	0.05
1,2,3,7,8-Penta-CCD*	2.00± 0.09	1.92± 0.09	0.58
1,2,3,4,7,8-Hexa-CCD*	1.88± 0.15	1.89± 0.10	0.93
1,2,3,6,7,8-Hexa-CCD*	3.78± 0.22	4.04± 0.09	0.29
1,2,3,7,8,9-Hexa-CCD*	2.05± 0.11	1.96± 0.09	0.53
1,2,3,4,6,7,8-Hepta-CCD*	4.35± 0.14	4.32± 0.09	0.84
OCDD*	6.34 ± 0.18	6.48 ± 0.12	0.49

[a] Adapted from Kang *et al.*, 2001.
[b] Mean of the natural log of the lipid adjusted concentration of analyte. Non-detects (31 0f 95) assigned 0.5 x LOD for geomean calculation.
[c] Student's-T-test used to compare mean values of exposure groups.

A second question addressed by Kang *et al.* (2001) was whether there were differences among members of the Army Chemical Corps who served duties in Vietnam but reported different levels of exposure when interviewed. The authors compared the geometric mean levels for TCDD according to 5 classifications of exposure (Table 6-9). The data in Table 6-9 refer only to concentrations of TCDD in the blood of Vietnam veterans who performed some type of activity that would have resulted in exposure to herbicide.

Table 6-9 Geometric Mean (GM) TCDD Concentrations (ln [TCDD] ppt, Lipid adjusted) in Blood of Vietnam Veterans Who Served in the Army Chemical Corps Between 1966 and 1971[a]

Self-reported exposure	Yes	No	P-values
	GM ± Standard error for ln [TCDD] ppt		
Sprayed Herbicide	1.33 ± 0.20	0.79 ± 0.18	0.05
Handled spray equipment	1.17 ± 0.18	0.86 ± 0.21	0.30
Present when others were spraying	1.15 ± 0.19	0.88 ± 0.20	0.34
Got herbicides on skin/clothing	1.19 ± 0.20	0.88 ± 0.19	0.26
Passed through defoliated areas	1.07 ± 0.17	0.97 ± 0.23	0.75

[a] Adapted from Kang *et al.*, 2001

Kang *et al*. (2001) concluded that there was no significant difference ($p>0.05$) in blood TCDD levels between members of the Army Chemical Corp indirectly associated with herbicide spraying (*e.g.*, handled spray equipment, present when others were spraying, got herbicide on skin/clothing, passed through defoliated areas) in Vietnam and members of the Army Chemical Corp that did not tour in Vietnam. Conversely, members of the Army Chemical Corp who sprayed herbicides in Vietnam had significantly elevated levels of TCDD in their blood.

Schecter *et al*. (2006) has reported that some Vietman verterans who were exposed to Agent Orange has TCDD levels as high as 600 ppt in lipid many years after leaving Vietnam. In 1989, Pirkle *et al.* reported the outcome of the analysis of serum concentrations of TCDD in 36 Ranch Hand veterans who had provided blood samples in 1982 and 1987. These determinations accurately reflected the concentration found in adipose tissue (Patterson *et al.*, 1988). This group was selected from a total of seventy-five veterans, approximately half of whom did not show evidence of levels of serum TCDD significantly different from background in the samples first taken in 1982 (Pirkle *et al.*, 1989). For the 36 veterans, the range of TCDD concentrations in 1982 was from 16.9 ppt to 423 ppt. Thirteen of these were ranked "high" at over 100 ppt. Although the accurate estimation of half-life would require more than two samples, the estimated first-order elimination rate was 7.1 years (95% confidence interval 5.8 to 9.6 years) (Pirkle *et al.*, 1989)

The Air Force Health Study of Ranch Hand veterans is a 20-year comprehensive assessment of the health of Air Force veterans of Operation Ranch Hand, the unit responsible for aerial spraying of herbicides in Vietnam. The study has compared the health and noncombat mortality of Ranch Hand veterans with a comparison group of Air Force veterans primarily involved with cargo missions in Southeast Asia but who were not exposed to herbicides (Wolfe *et al.*, 1990; Michalek *et al.*, 2001). The distribution of TCDD and the demographic characteristics of Ranch Hand veterans who served in Vietnam and the comparison group are shown in Table 6-10.

Table 6-10 Characteristics and Lipid Adjusted TCDD of U.S. Air Force Veterans in 1987[a]

Characteristic	Comparison[b]	Ranch Hand		
		Background [c]	Low exposure [d]	High exposure [e]
Number	1247	409	273	275
Mean TCDD [SD] ppt (1987)	4.6 [2.9]	5.8 [2.3]	15.6 [4.1]	69.4 [67.9]
Median (1987) ppt	4.1	5.7	14.7	45.7
Range (1987) ppt	0.4-54.8	0.6-10.0	10.0-25.6	18.0-617.8
Mean TCDD [SD] ppt (extrapolated)[f]	-	-	55.0 [18.0]	302.5 [327.3]
Median (extrapolated)	-	-	51.7	194.7
Range (extrapolated)	-	-	27.2-93.8	94-3290.2

[a] Adapted from Pavuk *et al.*, 2003.
[b] Comparison: veterans who served in Vietnam, participated in Operation Ranch Hand, served during the same period but never sprayed defoliants.
[c] Background category was mostly officers (TCDD [0.6 to 10 ppt]).
[d] Enlisted men; mostly air crew (TCDD [10.0 to 25.6 ppt]).
[e] Enlisted men; mostly ground crew (TCDD [18.0 to 617.8 ppt]).
[f] Back extrapolation was to last year of service and used a first order kinetics and a half-life for TCDD elimination of 8.7 years.

6.4 Summary of Selected TRVs

Table 6-11 contains a summary of TRVs selected for the purpose of this assessment. Details on the rational for the selection of these TRVs and details related to the endpoints of concern are provided in previous sections as well as in Appendix B.

Table 6-11 Summary of Selected TRVs

Chemical of Concern	TRV Type	TRV value	Source
Hexachlorobenzene	Acute	0.008 mg/kg	ATSDR
	Chronic non-cancer (TDI)	0.0005 mg/kg bw/day	Health Canada
	Chronic cancer (slope factor)	0.83 $(mg/kg\ bw/day)^{-1}$	Health Canada
Dioxin	Acute	200 pg TEQ/kg	ATSDR
	Chronic (TDI)	2.3 pg TEQ/kg bw/day	Health Canada
	Body $Burden_{TRV}$	27.8 pg TEQ/g lipid	based on Health Canada

7.0 RISK CHARACTERIZATION

The exposure assessment provided a plausible range of exposures for each receptor type. The range was described using three exposure estimates, including an upper, lower and, central estimate. The upper and lower estimates of exposure were intended to represent the extreme boundaries of plausible exposures, while the central tendency was considered the most likely case. Although risk characterization results are presented for the upper and lower boundaries, the central tendency represents the most plausible case and, therefore, the discussion and conclusions focuses around this scenario.

The risk characterization phase combines toxicity information with predicted exposure estimates. Typically, chronic and acute toxicity information is compared with corresponding chronic and acute exposure estimates to characterize long- and short-term health risks, respectively. Due to the persistent nature of the chemicals of concern, in addition to providing chronic and acute health risk estimates, a third scenario has been presented which compares short-term exposure rates to chronic toxicity data.

7.1 Dioxin Body Burden Calculations

As described in Section 5.0, a series of dioxin exposure estimates were generated for a number of different receptor groups. With the exception of the Trainee, each dioxin exposure estimate represents an absorbed dose resulting from a short exposure event. In an effort to examine the potential long-term human health risks associated with a short-term dioxin exposure event, dioxin body burden levels for a number of receptors were predicted over a 55 year period.

In an effort to approximate an individual's steady-state dioxin tissue concentration (or body burden), background exposure estimates of dioxin (on a pg TEQ/kg bw/day basis) were used to derived steady-state dioxin body burden concentrations on a pg dioxin per g lipid basis (pg TEQ/g lipid). A simple pharmacokinetic model provided by the U.S. EPA Dioxin Reassessment Manual (U.S. EPA, 2003) was used to relate the background daily intake of dioxin to a steady-state dioxin tissue concentration (pg TEQ/g lipid). The model is typically used to estimate intake rates based on measured dioxin tissue levels.

Equation 22

$$D = [(\ln 2/t_{1/2}) \times V \times CF_1 \times C \times CF_2] / A$$

where:

D	=	Daily intake of dioxin (pg TEQ/day)
$T_{1/2}$	=	Body half-life of dioxin (7.1 years)
V	=	Volume of fat in body (25% or 17.5 kg as per U.S. EPA, 2003)
C	=	Concentration of PCDD in human tissue (pg TEQ/g)
CF_1	=	1,000 g/kg
CF_2	=	years/ 365 days
A	=	Oral Absorption Factor (80% as per U.S. EPA, 2003)

The original equation provided by the U.S. EPA (2003) was re-arranged and solved for the parameter, "C". The receptor body weight was incorporated into the original equation to accommodate daily intake rates on a "ng TEQ/kg bw/day" basis.

Equation 23

$$C = \frac{D \times CF_3 \times A \times BW}{\left(\frac{\ln 2}{t_{1/2}}\right) \times V \times CF_1 \times CF_2}$$

where:

C	=	Concentration of PCDD in human tissue (72.5 pg TEQ/g)
D	=	Daily background PCDD TEQ intake (ng TEQ/kg bw/day)
$T_{1/2}$	=	Body half-life of dioxin (7.1 years)
V	=	Volume of fat in body (25% or 17.5 kg as per U.S. EPA, 2003)
CF_1	=	1,000 g/kg
CF_2	=	0.00274 years/day
CF_3	=	1,000 pg/ng
A	=	Absorption Factor (0.80 as per U.S. EPA, 2003)
BW	=	Body weight (70.7 kg)

This provided a steady-state background dioxin tissue concentration (on a pg TEQ/g lipid basis) as a function of reported background dioxin exposures (ng/day). For the general population in the mid 1960s, the background dioxin tissue concentration (or body burden) was estimated to be 72.5 pg TEQ/g lipid, based on a background exposure rate of 6.0 pg TEQ/kg bw/day dioxin (refer to Section 5.1.1 for a detailed discussion on background dioxin exposure rates). The background exposure rate was gradually lower between the years 1964 and 2021 (55 years) from a value of 6.0 pg TEQ/kg bw/day to 0.9 pg TEQ/kg bw/day. Prior to an acute dioxin exposure event taking place, a receptor's dioxin tissue concentration (or body burden) was assumed to be equal to that of the general population in the mid 1960s of 72.5 pg TEQ/g lipid.

The absorbed dose (as a result of an acute exposure event) was added to an individual's existing background or steady-state body burden of 72.5 pg TEQ/g lipid. The absorbed dose (resulting from the acute exposure event) was corrected for lipid content prior to adding it to the steady-state body burden concentration. As per the U.S. EPA (2003), the correction for lipid content involved the assumption that 25% of an individual's body weight (70.7 kg) is comprised of lipid and, therefore, a lipid volume of 17.5 kg was used. The absorbed dose (resulting from the acute exposure event) was therefore corrected for lipid content by applying a factor of 4.04 (*i.e.,* 70.7 kg body weight / 17.5 kg lipid) to the absorbed dose. The lipid-corrected dose resulting from an acute event was added to the steady-state body burden of 72.5 pg TEQ/g lipid. The day after the acute exposure event, the average daily intake of dioxin was assumed to return to a background rate.

As discussed in Section 5.1.1 and Appendix C, the average daily intake rate of dioxin among the general population is lower now than in the 1960s and early 1970s. As previously indicated, a background daily intake 6.0 pg TEQ/kg bw/day (equivalent to a steady-state body burden of 72.5 pg TEQ/g lipid) was assumed to represent an individual's average daily intake and body burden at the time of the spray events (1966-67). The background daily dioxin intake rate was

slowly decreased between the years of 1966 and 2021. Based on information reviewed to date (refer to Section 5.1.1 and Appendix C), the average daily dioxin intake rate was assumed to drop from 6.0 pg TEQ/kg bw/day to 0.9 pg TEQ/kg bw/day between 1966 and today.

Using a body burden half life of 7.1 years (Pirkle *et al*., 1989; Wolfe *et al*., 1988; Aylward *et al.,* 2005) and a decreasing background daily intake, dioxin tissue concentrations were predicted from the initial acute exposure event (*e.g*., June, 1966) to the year 2021. The initial dioxin tissue concentration at the time of the acute exposure event was calculated as follows:

Equation 24

$$BB_o = BBB + BB_{event}$$

where:

BB_o (pg TEQ/g lipid)	=	Total body burden as a result of a one day exposure event plus background
BBB	=	Background body burden (72.5 pg TEQ/g lipid)
BB_{event}	=	Body burden due to a one day exposure event (pg TEQ/g lipid)

Equation 25

where:

$$BB_{event} = ABD_{acute} \text{ x } ND \times BW / V$$

BB_{event}	=	Body burden resulting from a one day exposure event (pg TEQ/g lipid)
ABD_{acute}	=	Absorbed dose from a one day exposure event (ng TEQ/kg bw/day)
ND	=	Number of days (1 day)
BW	=	Body weight of 70.7 kg (Health Canada, 2004)
V	=	Volume of fat in the body 17.5 kg (U.S. EPA, 2003)

Equation 24 combines the PCDD background body burden concentration of 72.5 (pg TEQ / g lipid) and the absorbed dose resulting from a one day exposure event. With the exception of the Trainee, each dioxin exposure estimate represents an absorbed dose resulting from a one-day exposure event. It was assumed that all plots sprayed with Agent Orange, Purple or some other mixture containing 2,4,5-T and, therefore, potentially contaminated with PCDD were completed in one day.

As previously discussed in Section 5.1, the background PCDD body burden of the general population has slowly declined between the mid-1960s and present day. The value referred to above represents the background PCDD body burden of an individual during the 1960s. Refer to Section 5.1 and Appendix C for a detailed discussion regarding background exposure rates to dioxin like compounds. The estimated absorbed dose was corrected for lipid content as per U.S. EPA, 2003. It is noted that ABD_{acute} represents the predicted exposures presented in Tables 5-14

through 5-19. These exposure estimates represent an absorbed dose, not an applied dose and, therefore, a correction for lipid content was applied directly to these values.
Based on a body burden half-life of 7.1 years and a background daily intake of dioxin, body burden levels were calculated on a yearly basis until the year 2021. Using the first-order rate law and a body burden half-life of 7.1 years, the body burden one year after the acute one-day exposure event in 1966 was predicted using the following:

Equation 26

$$BB_{year\ 1} = BBB + (BB_{event} e^{-kt})$$

where:

$BB_{year\ 1}$	=	Body burden one year after the acute exposure event (pg TEQ/g lipid)
BBB	=	Background body burden (72.5 pg TEQ/g lipid)
BB_{event}	=	Body burden as a result of a one day exposure event (pg TEQ/g lipid)
k	=	rate constant (0.0003 $days^{-1}$)
t	=	time (365 days)

Equation 27

where:

$$k = \frac{\ln 2}{t_{1/2}}$$

where:

ln 2	=	natural log of 2
$t_{1/2}$	=	half-life of 2,3,7,8-TCDD (2591.5 days or 7.1 years)

Equation 26 calculates the PCDD body burden concentration one year after the initial acute exposure event. Again, the background body burden is added the event-specific body burden value which was decayed, assuming a half-life of 7.1 years. The one-year elimination term, as described above would be equal to e^{-kt}; where t is equal to one year or 365 days. Similar calculations were conducted for all subsequent years using Microsoft Excel©.

Table 7-1 provides an example of the datasheet used to calculate dioxin body burdens from 1964 to 2021 for a Mixer/Loader wearing a single layer of clothing and gloves (central exposure estimate) under routine conditions only.

As illustrated in Table 7-1, the background daily intake for dioxin decreases from an initial daily intake rate of 6.0 pg TEQ/kg bw/day (equivalent to a daily absorbed dose of 4.8 pg TEQ/kg bw/day) to a daily intake of 0.9 pg TEQ/kg bw/day (or 0.72 pg TEQ/kg bw/day absorbed dose). It was assumed that this decrease occurs gradually over time and follows the trend noted in Table 7-1. A general absorption factor of 80% was used as per U.S. EPA (2003) to determine the absorbed dose. Refer to Section 5.1 for a discussion of historical background PCDD exposure

rates. Appendix E provides a "Worked Example" including input parameters and calculated results from Equations 22 through 27.

Table 7-1 Example Data Sheet for Body Burden Calculations

Mixer/Loader - Single Layer with Gloves (Central Exposure Estimate)			
Year	**Absorbed Dose (pg TEQ/kg bw/day)**	**Mixer/Loader Total Body Burden (pg TEQ/g lipid)**	**Event-Specific Body Burden (pg TEQ/g lipid)**
1964	4.8	72.5	0.00
1965	4.8	72.5	0.00
1966 – a single exposure event	372.6	74.0	1.51
1967	4.8	73.9	1.37
1968	4.8	73.7	1.24
1969	4.8	73.6	1.12
1970	4.8	73.5	1.02
1971	4.4	67.4	0.92
1972	4.4	67.3	0.84
1973	4.4	67.2	0.76
1974	4.4	67.2	0.69
1975	4.0	61.1	0.63
1976	3.6	54.9	0.57
1977	3.6	54.9	0.51
1978	3.2	48.8	0.47
1979	3.2	48.8	0.42
1980	2.8	42.7	0.38
1981	2.8	42.6	0.35
1982	2.4	36.6	0.32
1983	2.4	36.5	0.29
1984	2.0	30.5	0.26
1985	1.6	24.4	0.24
1986	1.4	21.4	0.21
1987	1.4	21.3	0.19
1988	1.4	21.3	0.18
1989	1.4	21.3	0.16
1990	1.4	21.3	0.14
1991	1.4	21.3	0.13
1992	1.4	21.3	0.12
1993	1.4	21.3	0.11
1994	1.4	21.2	0.10
1995	1.4	21.2	0.09
1996	1.2	18.2	0.08
1997	1.2	18.2	0.07
1998	1.2	18.2	0.07
1999	0.8	12.1	0.06
2000	0.8	12.1	0.05
2001	0.7	10.9	0.05
2002	0.7	10.9	0.04
2003	0.7	10.9	0.04
2004	0.7	10.9	0.04

Table 7-1 Example Data Sheet for Body Burden Calculations

Mixer/Loader - Single Layer with Gloves (Central Exposure Estimate)			
Year	**Absorbed Dose (pg TEQ/kg bw/day)**	**Mixer/Loader Total Body Burden (pg TEQ/g lipid)**	**Event-Specific Body Burden (pg TEQ/g lipid)**
2005	0.7	10.9	0.03
2006	0.7	10.9	0.03
2007	0.7	10.9	0.03
2008	0.7	10.9	0.02
2009	0.7	10.9	0.02
2010	0.7	10.9	0.02
2011	0.7	10.9	0.02
2012	0.7	10.9	0.02
2013	0.7	10.9	0.02
2014	0.7	10.9	0.01
2015	0.7	10.9	0.01
2016	0.7	10.9	0.01
2017	0.7	10.9	0.01
2018	0.7	10.9	0.01
2019	0.7	10.9	0.01
2020	0.7	10.9	0.01
2021	0.7	10.9	0.01

The absorbed dose (pg TEQ/kg bw/day) presented in the 1966 row does not represent the average daily intake over the year of 1966, but rather a one day exposure event. As previously discussed, 45 plots in 1966 were identified as being potentially contaminated with PCDD. It was assumed that all plots sprayed with Agent Orange, Purple or some other mixture containing 2,4,5-T were completed in a single 12-hour shift. This would leave 2 days to complete the remaining 71 plots. The second column entitled the "Mixer/Loader Total Body Burden (pg TEQ/g lipid)" represents the sum of the predicted background body burden (72.5 pg TEQ/g lipid) plus the event-specific body burden (1.51 pg TEQ/g lipid). In the 1967 row, the value in the "Mixer/Loader Total Body Burden (pg TEQ/g lipid)" column represents the background body burden (72.5 pg TEQ/g lipid) plus the event-specific body burden which has been multiplied by the decay constant (e^{-kt}; where t is 365 days). This process continues for each subsequent year using the event-specific body burden from each previous year.

7.2 Dioxin Risk Characterization

7.2.1 Acute Risk/Acute Exposure

Tables 7-2 through 7-8 provide short-term risk estimates for all short-term or acute exposure scenarios. Several risk estimates exceed the benchmark (HQ > 1), and as such require further consideration. With the exception of the Applicator scenario, the short-term HQ values for all exposure scenarios (under the central exposure estimate) were greater than a value of 1.0, indicating that the central exposure estimates exceeded the acute TRV (200 pg TEQ/kg bw/day). Low and high risk estimates are provided (facilitated through the use of selected low and high exposure input parameters) to give a general appreciation for the level of uncertainty and variability present within the quantitative risk estimates. Due to lack of repetitive input parameter

selection bias utilized for both the high- and low-case exposure estimates, it was felt that central estimates were the most realistic and, therefore, further discussions focus on these risk estimates.

A HQ value greater than 1.0 does not indicate that adverse health effects would have occurred; however, it does indicate that some receptors may have experienced elevated exposures and as such, the potential for elevated risks. It is also important to understand how risks related to the herbicide spray activities compare with those experienced by people not involved with or impacted by herbicide spray activities at CFB Gagetown (*i.e.*, background). Tables 7-2 through 7-8 provide background, or non-site related, risk estimates for the 1960s. Background exposures predicted for the 1960's were substantially higher than those experienced today (see Table 5-1) and in fact exceed acceptable levels by today's standards. Only those exposure estimates associated with the two accident scenarios (spill and direct spray) and routine flagging activities (alternate method) exceeded both the risk benchmark and the background exposure estimate for the 1960's. Flagger risk estimates derived using the PHED method were within acceptable levels. Two approaches were used to estimate exposures for the flagger. In addition to the PHED method, it was considered appropriate to apply traditional quantitative exposure methods to these types of exposures. The exposure estimates developed through the use of traditional quantitative methods are much greater than those produced by the PHED approach. The difference observed between the two methods is considered a significant uncertainty.

The two accident scenarios are clearly extreme cases; however, it is unknown whether these types of incidental exposures actually occurred during the 1966/67 trials. In the absence of any information to suggest otherwise, it is only reasonable to assume these types of accidental spills and/or spray events occurred. It is recognized that the exposure estimates resulting from the two accident scenarios are significantly greater from those generated using the PHED approach. Although it has been suggested that the PHED approach inherently accounts for accidental exposures, the details with respect to this methodology are not known. It is unclear how the application practices of the last 10 to 20 years compares with the activities of the 1966 and 1967 trials and it is unclear how the accident data included in the PHED values have been incorporated into the final exposure estimates. Although PHED data would inherently include the frequency and magnitude of accidental exposures over a prolonged period of time, the exposure event of concern occurred over a one day period and, therefore, may not be comparable to the long-term exposure duration of a pesticide applicator..

With the exception of two accident scenarios, the acute risks predicted through this evaluation have been classified as "less serious" by ATSDR (see Section 6.2.2). "Serious" effects were not noted until exposures of more than 300-fold greater than the acute TRV. These "less serious" exposure levels are not indicative of elevated risks of long-term irreversible health effects, rather, the potential for short-term reversible effects, of the nature considered "less serious" by ATSDR. Risk estimates predicted for the accident scenarios are indicative of potentially 'serious' effects; however, the occurrence of accidents of this nature during the 1966 and 1967 spray periods remains uncertain. While elevated risks do not necessarily equate to certain effects it does raise the level of concern and indicates that further epidemiological investigation of individuals involved in these operations is warranted.

The potential for long-term effects are evaluated further in Section 7.2.3.

Table 7-2 Acute Hazard Quotients for the Mixer/Loader

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
Routine 1966	1.1E-02	1.8E-01	2.1E+02	5.0E-01	1.7E+00	**3.4E+00**	5.5E-01	1.9E+00	**2.2E+02**
Accident 1966	**3.3E+02**	**3.3E+03**	**2.2E+04**	-	-	-	**3.3E+02**	**3.3E+03**	**2.2E+04**
Total 1966	**3.3E+02**	**3.3E+03**	**2.2E+04**	5.0E-01	**1.7E+00**	**3.4E+00**	**3.3E+02**	**3.3E+03**	**2.2E+04**
Routine 1967	2.6E-04	1.2E-02	**4.3E+01**	1.1E-02	9.5E-02	6.0E-01	0.0E+00	1.0E-01	4.3E+01
Accident 1967	**1.9E+01**	**4.0E+02**	**9.5E+03**	-	-	-	**1.9E+01**	**4.0E+02**	**9.5E+03**
Total 1967	**1.9E+01**	**4.0E+02**	**9.5E+03**	1.1E-02	9.5E-02	6.0E-01	**1.9E+01**	**4.0E+02**	**9.5E+03**

Bolded values indicate an exceedance of the acceptable risk benchmark (1.0)
Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

Table 7-3 Acute Hazard Quotients for the Applicator

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
1966	2.3E-03	3.7E-02	3.3E-01	2.3E-02	7.5E-02	1.5E-01	2.5E-02	1.1E-01	4.8E-01
1967	5.5E-05	2.4E-03	6.5E-02	4.8E-04	4.3E-03	2.6E-02	0.0E+00	5.0E-03	9.0E-02

[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

Table 7-4 Acute Hazard Quotients for the Flagger (PHED Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
Routine 1966	5.0E-03	6.5E-02	8.5E-01	1.7E-01	5.5E-01	1.1E+00	1.8E-01	6.5E-01	2.0E+00
Routine 1967	1.1E-04	3.7E-03	1.5E-01	3.6E-03	3.2E-02	2.0E-01	3.7E-03	3.6E-02	3.4E-01

Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

Table 7-5 Acute Hazard Quotients for the Flagger (Alternate Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
Routine 1966	1.5E+00	**5.5E+01**	**1.4E+03**	-	-	-	1.5E+00	**5.5E+01**	**1.4E+03**
Routine 1967	2.9E-02	3.0E+00	2.2E+02	-	-	-	2.9E-02	3.0E+00	2.2E+02

Bolded values indicate an exceedance of the acceptable risk benchmark (1.0)
Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

Table 7-6 Acute Hazard Quotients for the Field Scout

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
1966	1.0E-01	1.6E+00	**4.3E+01**	-	-	-	1.0E-01	1.6E+00	**4.3E+01**
1967	1.6E-03	7.0E-02	**6.5E+00**	-	-	-	1.6E-03	7.0E-02	**6.5E+00**

Bolded values indicate an exceedance of the acceptable risk benchmark (1.0)
Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

Table 7-7 Acute Hazard Quotients for the Flagger/Trainee following a Spray Accident

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]								**2.6E+00**	
Accident 1966	**6.0E+00**	**1.1E+02**	**1.2E+03**	-	-	-	**6.0E+00**	**1.1E+02**	**1.2E+03**
Accident 1967	2.9E-01	**1.1E+01**	**4.4E+02**	-	-	-	2.9E-01	**1.1E+01**	**4.4E+02**

Bolded values indicate an exceedance of the acceptable risk benchmark (1.0)
Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

7.2.2 Chronic Risk/Chronic Exposure

Table 7-8 provides long-term risk estimates for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas for a three year period following the spray applications. Table 7-8 also provide a comparison to background, or non-site related, risks estimated for the 1960s. All site-related risk estimates are less than levels that are indicative of a concern (HQ < 1). Additionally, all risk estimates are less than background risk estimates.

Table 7-8 Chronic Hazard Quotients for the Trainee (dioxins)

Chemical	Exposure *via* Direct Dermal Contact			Exposure *via* Incidental Soil Ingestion and Wild Berry Consumption			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
DIOXIN									
background (non-site related)[a]							2.6E+00		
1966	6.5E-04	3.8E-03	1.3E-02	1.1E-03	6.5E-03	2.2E-02	1.8E-03	1.0E-02	3.5E-02
1967	8.0E-05	1.3E-03	1.3E-02	1.4E-04	2.2E-03	2.3E-02	2.2E-04	3.5E-03	3.5E-02

[a] Background risks calculated based on the EDI estimated for 1966 (6.0 pg/kg bw/day) and the TRV of 2.3 pg/kg bw/day

7.2.3 Chronic Risk/Acute Exposure

As discussed in Section 3.4.2, for chemicals like dioxin, that are persistent within the body, there is a potential for very high short-term exposures to remain in the body and result in long-term health effects. Tables 7-9 and 7-10 demonstrate predicted dioxin body burdens at several intervals following the spray events. Figures 7-1 through 7-5, demonstrate this information on a year to year basis several situations where the Body Burden$_{TRV}$ is exceeded. A comparison to background or non-site related exposures is also provided in Tables 7-9 and 7-10, and Figures 7-1 through 7-5. Body Burden$_{TRV}$ exceedances are indicative of elevated dioxin levels within the body long after the acute exposure event. The elevated dioxins levels are indicative of an elevated risk for adverse chronic health effects. While elevated risks does not equate to a certain effect it does raise the level of concern and indicates that further epidemiological investigations of individuals who potentially experienced these acute exposures is warranted. As indicated previously, background exposures predicted for the 1960's were substantially higher than those experienced today, and in fact, exceed acceptable levels by today's standards. As indicted in Tables 7-9 and 7-10, body burdens predicted for the accident scenarios (mixer/loader spill accident and flagger/trainee spray accident) substantially differ from those related to background. The results of the assessment indicated that elevated dioxin body burdens will have persisted in persons experiencing these exposures (*i.e.*, accidental exposures) for as many as 52 years following the spray events. In other words, it was estimated that it would take approximately 52 years after the accident to reach the Body Burden$_{TRV}$ of 27.8 pg TEQ/g, relative to 17.5 years for a background individual (*i.e.*, an individual not involved with spraying activities at CFB Gagetown). Body burdens estimated for all other exposure scenarios differ only marginally from those predicted for background exposures.

The results of this assessment are quite comparable to estimates for the Ranch Hand veterans who served in Vietnam (Table 7-11). The 1987/88 measured body burdens of Ranch Hand veterans who served in Vietnam during the 1960s are comparable to the predicted body burden

levels in 1987/88 (*i.e.*, approximately 20 years after the event) of individuals involved in the CFB Gagetown trials of 1966/67. For the purpose of this comparison, Low Exposures have been considered equivalent to those experienced during routine spraying events, while High Exposures have been considered equivalent to those experienced following accidental spray events.

Table 7-9 Predicted dioxin Body Burdens (pg TEQ/g lipid) From the 1966 Spray Campaign

Exposure Scenario	Day 1 (1966)	Year 1 (1966)	Year 10 (1976)	Year 20 (1986)	# of Years to Reach a Body $Burden_{TRV}$ (27.8 pg TEQ/g)
	pg TEQ/g lipid				
Mixer/Loader central estimate – routine exposures	74.0	73.9	54.9	21.4	17.5
Mixer/Loader central estimate – routine plus accident exposures	2,687	2,444	1,146	392	52
Flagger central estimate – routine exposures	73.0	73.0	54.6	21.2	18.5
Flagger/Trainee – central estimate – routine plus accident exposures (spray accident)	157	149	86.3	33.2	26
Scout – central estimate	73.8	73.7	54.9	21.3	17.5
Military Trainee – central estimate	72.5	72.5	54.4	21.2	17.5
Background Individual	72.5	72.5	54.4	21.1	17.5

Table 7-10 Predicted dioxin Body Burdens (pg TEQ/g lipid) From the 1967 Spray Campaign

Exposure Scenario	Day 1 (1967)	Year 1 (1967)	Year 10 (1977)	Year 20 (1987)	# of Years to Reach a Body $Burden_{TRV}$ (27.8 pg TEQ/g)
	pg TEQ/g lipid				
Mixer/Loader central estimate – routine exposures	72.6	72.6	54.4	21.2	17.5
Mixer/Loader central estimate – routine plus accident exposures	393	363	175	66.7	31.5
Flagger central estimate – routine exposures	72.5	72.5	54.4	21.2	17.5
Flagger/Trainee – central estimate – routine plus accident exposures (spray accident)	81.5	80.7	57.8	22.4	17.5
Scout – central estimate	72.6	72.6	54.4	21.2	17.5
Military Trainee – central estimate	72.5	72.5	54.4	21.2	17.5
Background Individual	72.5	72.5	54.4	21.1	17.5

Table 7-11 Comparison of TCDD Body Burdens – Ranch Hand Veterans Personnel Individuals Involved with 1966/1967 Spray Activities at CFB Gagetown

Characteristic	CFB Gagetown		Ranch Hand[a]	
	Routine Exposures[b]	Accidental Exposures[c]	Low exposure[d]	High exposure[e]
1987/88 (pg TEQ/g lipid)[f]	21.2-21.4	22.4-392	10.0-25.6	18.0-617.8
1966/67 (pg TEQ/g lipid)[g]	72.5-74	81.5-2687	27.2-93.8	94-3290.2

[a] Adapted from Pavuk *et al.*, 2003.
[b] Routine exposures include mixer/loader, applicator, flagger, scout and military trainee
[c] Accidental exposures include mixer/loader spill accident and flagger/trainee direct spray accident
[d] Enlisted men; mostly air crew .
[e] Enlisted men; mostly ground crew.
[f] 1987/88 body burdens estimated for CFB Gagetown and measured for Ranch Hand in 1987.
[g] 1966/67 body burdens estimated for CFB Gagetown and back extrapolated for Ranch Hand to last year of service.

Figure 7-1 PCDD Body Burden (pg TEQ/g lipid) *Versus* Time (years) – 1966 Spray Campaign – Mixer/Loader Central Estimate - Routine Plus Accident Exposures

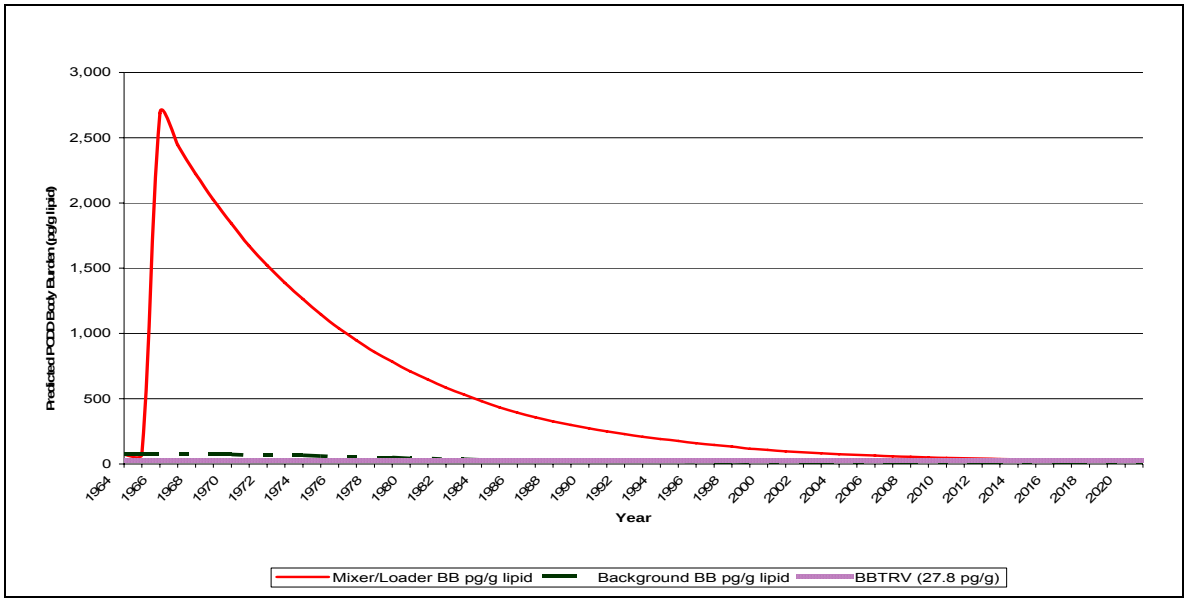


Figure 7-2 PCDD Body Burden (pg TEQ/g lipid) *Versus* Time (years) – 1966 Spray Campaign – Flagger/Trainee Central Estimate (PHED DATA) - Spray Accident Exposures

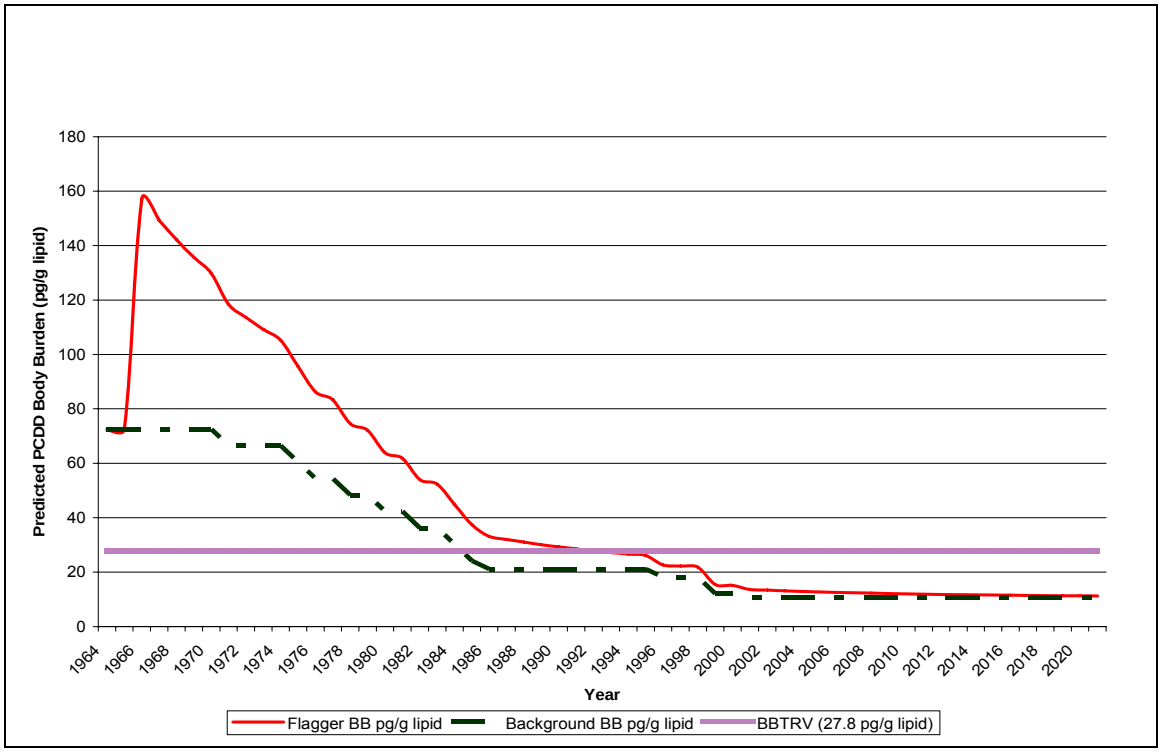


Figure 7-3 PCDD Body Burden (pg TEQ/g lipid) *Versus* Time (years) – 1967 Spray Campaign – Mixer/Loader Central Estimate - Routine Plus Accident Exposures

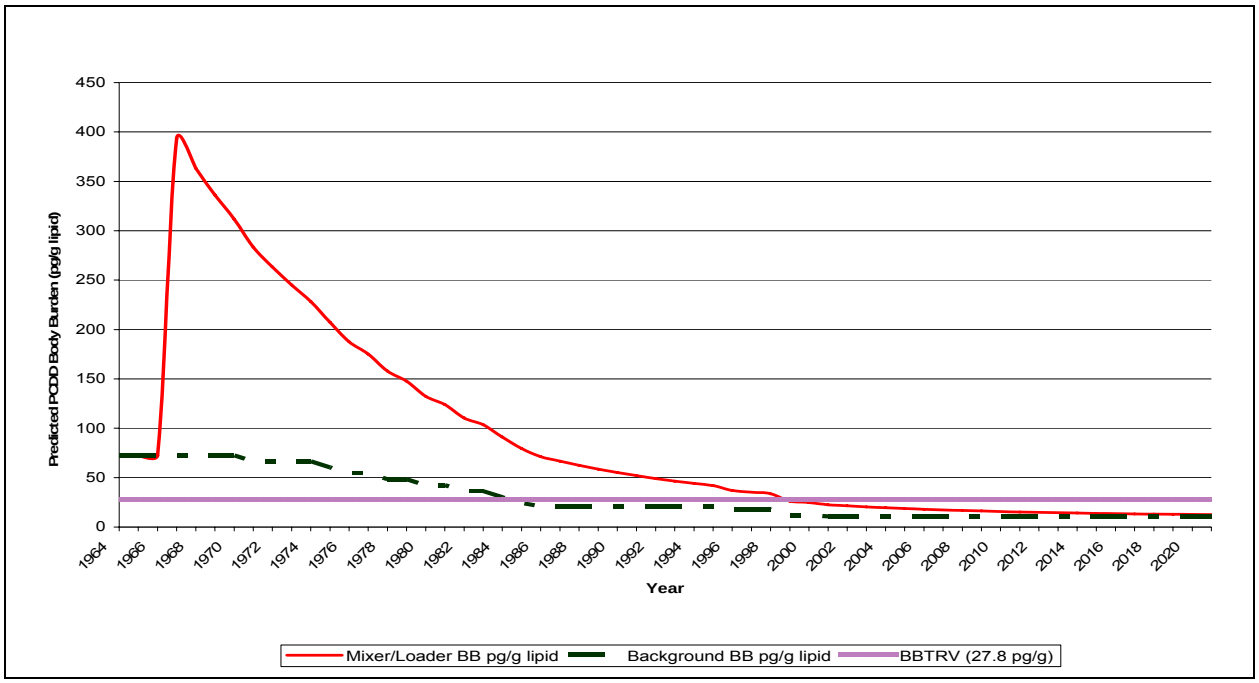


Figure 7-4 PCDD Body Burden (pg TEQ/g lipid) *Versus* Time (years) – 1967 Spray Campaign – Flagger/Trainee Central Estimate (PHED DATA) – Routine plus Spray Accident Exposures

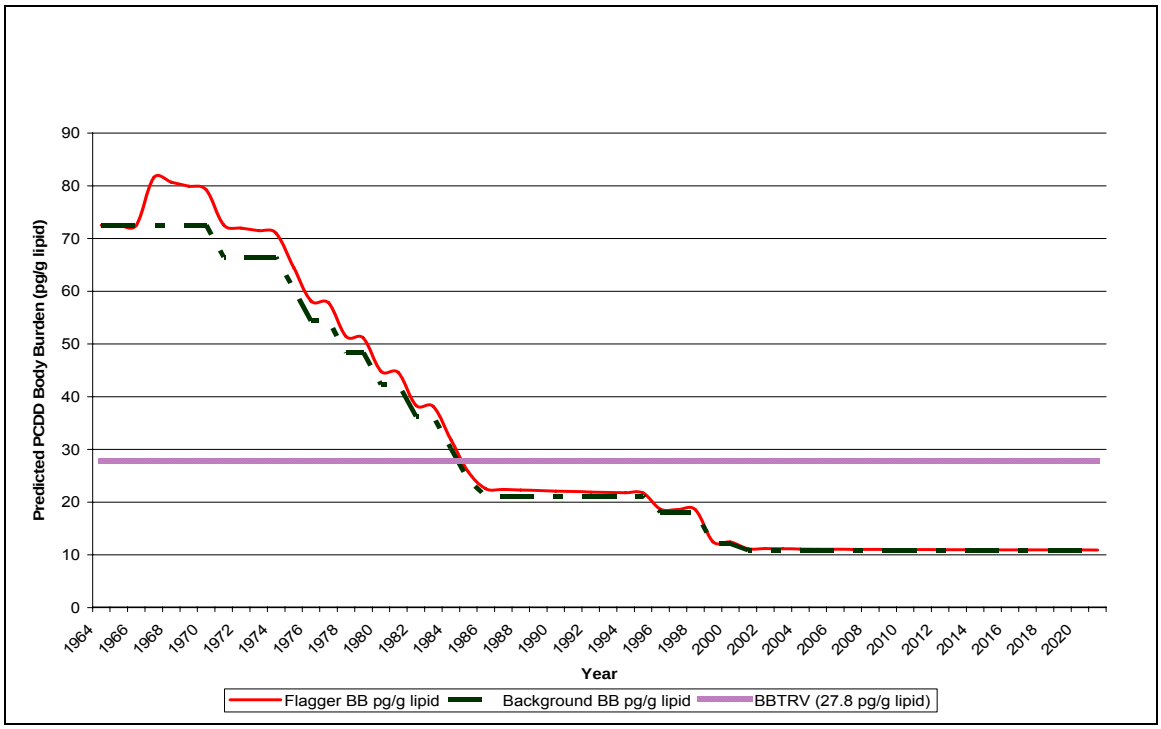
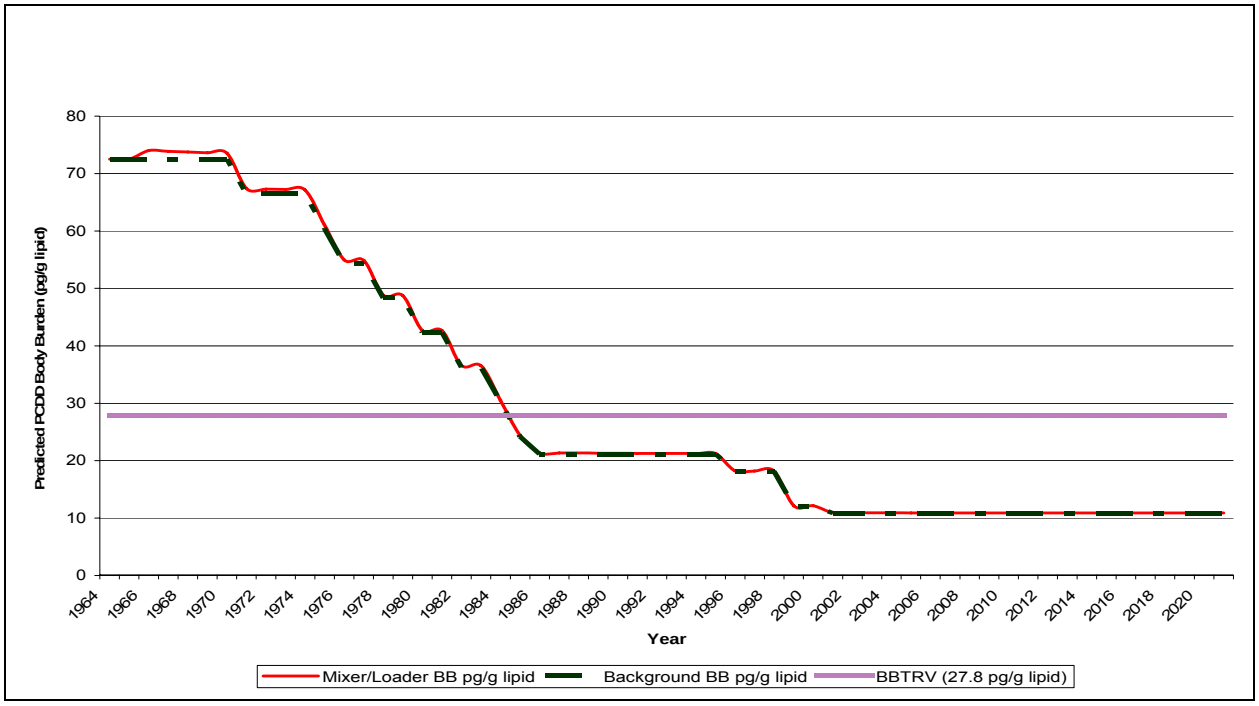


Figure 7-5 PCDD Body Burden (pg TEQ/g lipid) *Versus* Time (years) – 1966 Spray Campaign – Mixer/Loader Central Estimate - Routine Exposures



7.3 Hexachlorobenzene (HCB)

7.3.1 Acute Risk/Acute Exposure

Tables 7-12 through 7-17 provide short-term risk estimates for all short-term or acute exposure scenarios. Tables 7-12 through 7-17 also provide a comparison to background, or non-site related, risks estimated for the 1960s. All risk estimates are less than levels that are indicative of a concern (HQ < 1). Total risks can be estimated by combining site-related risk estimates and background risk estimates. Since background risks are 1,000-fold less than the HQ benchmark, addition of site-related risks and background risks will not impact the results of this assessment.

Table 7-12 Acute Hazard Quotients for the Mixer/Loader

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
Routine 1966	4.3E-07	2.8E-06	1.4E-03	1.9E-05	2.9E-05	2.9E-05	1.9E-05	3.1E-05	1.4E-03
Accident 1966	1.1E-02	4.3E-02	1.8E-01	-	-	-	1.1E-02	4.3E-02	1.8E-01
Total 1966	1.1E-02	4.3E-02	1.8E-01	1.9E-05	2.9E-05	2.9E-05	1.1E-02	4.3E-02	1.8E-01
Routine 1967	1.0E-06	6.5E-06	3.3E-03	4.4E-05	6.9E-05	6.9E-05	4.5E-05	7.5E-05	3.3E-03
Accident 1967	2.1E-02	8.6E-02	3.4E-01	-	-	-	2.1E-02	8.6E-02	3.4E-01
Total 1967	2.1E-02	8.6E-02	3.5E-01	4.4E-05	6.9E-05	6.9E-05	2.1E-02	8.6E-02	3.5E-01

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

Table 7-13 Acute Hazard Quotients for the Applicator

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
1966	9.3E-08	5.8E-07	2.1E-06	8.1E-07	1.3E-06	1.3E-06	8.8E-07	1.9E-06	3.4E-06
1967	2.3E-07	1.4E-06	4.9E-06	1.9E-06	3.0E-06	3.0E-06	2.1E-06	4.4E-06	7.9E-06

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

Table 7-14 Acute Hazard Quotients for the Flagger (PHED Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
Routine 1966	2.5E-07	1.0E-06	5.3E-06	6.0E-06	9.6E-06	9.6E-06	6.3E-06	1.1E-05	1.5E-05
Routine 1967	5.0E-07	2.4E-06	1.2E-05	1.5E-05	2.3E-05	2.3E-05	1.5E-05	2.5E-05	3.5E-05

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

Table 7-15 Acute Hazard Quotients for the Flagger (Alternate Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
Routine 1966	6.1E-05	9.0E-04	8.6E-03	-	-	-	6.1E-05	9.0E-04	8.6E-03
Routine 1967	1.4E-04	2.0E-03	1.9E-02	-	-	-	1.4E-04	2.0E-03	1.9E-02

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

Table 7-16 Acute Hazard Quotients for the Field Scout

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
1966	3.8E-06	2.4E-05	2.6E-04	-	-	-	3.8E-06	2.4E-05	2.6E-04
1967	1.0E-05	5.6E-05	6.1E-04	-	-	-	1.0E-05	5.6E-05	6.1E-04

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

Table 7-17 Acute Hazard Quotients for the Flagger/Trainee following a Spray Accident

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							7.75E-04		
Accident 1966	1.3E-04	9.3E-04	5.9E-03	-	-	-	1.3E-04	9.3E-04	5.9E-03
Accident 1967	3.8E-04	2.8E-03	1.8E-02	-	-	-	3.8E-04	2.8E-03	5.4E-02

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the acute TRV of 8,000 ng/kg bw/day

7.3.2 Chronic Risk/Chronic Exposure

Tables 7-18 and 7-19 provide chronic risk estimates (for cancer and non-cancer endpoints) for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas more than a year following the spray applications. Tables 7-18 through 7-19 also provide a comparison to background, or non-site related, risks estimated for the 1960s. All risk estimates are less than levels that are indicative of a concern (HQ < 1 and ILCR < 10^{-5} or 1/100,000)

Table 7-18 Chronic Hazard Quotients (non-cancer endpoints) for the Trainee

Chemical	Exposure *via* Direct Dermal Contact			Exposure *via* Incidental Soil Ingestion and Wild Berry Consumption			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							1.24E-02		
1966	1.1E-07	2.6E-07	4.0E-07	2.0E-08	4.7E-08	7.3E-08	1.4E-07	3.0E-07	4.7E-07
1967	3.5E-07	8.2E-07	1.3E-06	5.2E-08	1.2E-07	1.8E-07	4.2E-07	9.6E-07	1.5E-06

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the chronic TRV of 500 ng/kg bw/day

Table 7-19 ILCR Estimates (cancer endpoints) for the Trainee

Chemical	Exposure *via* Direct Dermal Contact			Exposure *via* Incidental Soil Ingestion and Wild Berry Consumption			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							5.15E-06		
1966	3.2E-12	7.1E-12	1.1E-11	5.6E-13	1.3E-12	2.0E-12	3.8E-12	8.4E-12	1.3E-11
1967	9.7E-12	2.3E-11	3.5E-11	1.4E-12	3.3E-12	5.0E-12	1.2E-11	2.7E-11	4.0E-11

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

7.3.3 Chronic Risk/Acute Exposure

Tables 7-20 through 7-25 provide carcinogenic risk estimates for all acute exposure scenarios. With the exception of the mixer/loader accident scenario, all risk estimates are less than levels that are indicative of a concern (HQ < 1 and ILCR < 10^{-5} or 1/100,000). ILCR estimates marginally exceed the 10^{-5} benchmark for the high end (worst case) mixer/loader accident scenario. ILCR estimates for the central tendency receptor are essential equivalent to the benchmark for the 1967 spray period. These risk estimates assume the potential for an increased cancer risk following a one-hit exposure. As discussed in Section 3.4.2, the evaluation of cancer risks following acute duration exposures is an area of high uncertainty and questionable relevance. Given the marginal exceedances estimated and the highly conservative nature of this evaluation, these exceedances are not considered significant or indicative of an elevated cancer risk.

Table 7-20 ILCR Estimates for the Mixer/Loader Following Acute Exposure

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]								5.15E-06	
Routine 1966	4.4E-11	2.8E-10	1.4E-07	1.9E-09	3.0E-09	3.0E-09	1.9E-09	3.2E-09	1.4E-07
Accident 1966	1.1E-06	4.4E-06	**1.8E-05**	-	-	-	1.1E-06	4.4E-06	**1.8E-05**
Total 1966	1.1E-06	4.4E-06	**1.8E-05**	1.9E-09	3.0E-09	3.0E-09	1.1E-06	4.4E-06	**1.8E-05**
Routine 1967	1.0E-10	6.7E-10	3.4E-07	4.5E-09	7.1E-09	7.1E-09	4.7E-09	7.8E-09	3.4E-07
Accident 1967	2.2E-06	8.9E-06	**3.5E-05**	-	-	-	2.2E-06	8.9E-06	**3.5E-05**
Total 1967	2.2E-06	8.9E-06	**3.6E-05**	4.5E-09	7.1E-09	7.1E-09	2.2E-06	8.9E-06	**3.6E-05**

Bolded values indicated an exceedance of the acceptable risk benchmark (1.0E-05)
Underlined values indicate an exceedance of background risk estimates
[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

Table 7-21 ILCR Estimates for the Applicator Following Acute Exposure

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]								5.15E-06	
1966	1.0E-11	6.4E-11	2.4E-10	9.0E-11	1.4E-10	1.4E-10	9.7E-11	2.1E-10	3.7E-10
1967	2.5E-11	1.5E-10	5.4E-10	2.1E-10	3.3E-10	3.3E-10	2.4E-10	4.9E-10	8.7E-10

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

Table 7-22 ILCR Estimates for the Flagger Following Acute Exposure (PHED Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							5.15E-06		
Routine 1966	2.8E-11	1.1E-10	5.8E-10	6.7E-10	1.1E-09	1.1E-09	6.9E-10	1.2E-09	1.7E-09
Routine 1967	5.5E-11	2.6E-10	1.4E-09	1.7E-09	2.5E-09	2.5E-09	1.7E-09	2.8E-09	3.9E-09

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

Table 7-23 ILCR Estimates for the Flagger Following Acute Exposure (Alternate Method)

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							5.15E-06		
Routine 1966	6.8E-09	1.0E-07	9.6E-07	-	-	-	6.8E-09	1.0E-07	9.6E-07
Routine 1967	1.5E-08	2.2E-07	2.1E-06	-	-	-	1.5E-08	2.2E-07	2.1E-06

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

Table 7-24 ILCR Estimates for the Field Scout Following Acute Exposure

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							5.15E-06		
1966	4.2E-10	2.6E-09	2.9E-08	-	-	-	4.2E-10	2.6E-09	2.9E-08
1967	1.1E-09	6.2E-09	6.8E-08	-	-	-	1.1E-09	6.2E-09	6.8E-08

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

Table 7-25 ILCR Estimates for the Flagger/Trainee following a Spray Accident

Chemical	Dermal Exposure			Inhalation Exposure			Total Exposure		
	Low	Central	High	Low	Central	High	Low	Central	High
HCB									
background (non-site related)[a]							5.15E-06		
Accident 1966	1.4E-08	1.0E-07	6.5E-07	-	-	-	1.4E-08	1.0E-07	6.5E-07
Accident 1967	4.2E-08	3.0E-07	1.9E-06	-	-	-	4.2E-08	3.0E-07	1.9E-06

[a] Background risks calculated based on the EDI estimated for 1966 (6.2 ng/kg bw/day) and the slope factor of 0.83 $(mg/kg\ bw/day)^{-1}$ or 8.3E-07 $(ng/kg\ bw/day)^{-1}$

8.0 UNCERTAINTIES

Quantitative human health risk assessment generally involves assigning numerical values to input parameters in an appropriate exposure or risk model to obtain a quantitative estimate of risk. Numerical values are required for parameters describing contaminant concentrations in environmental media, contaminant fate and transport, human exposure and toxic response. These values may be measured, assumed, prescribed or based on published literature. Variability and uncertainty in the input parameters or risk model result in variability and uncertainty in the estimate of risk. U.S. EPA (2000) advocates that the risk characterization process maintains transparency, clarity, consistency, and reasonableness. The goal of risk characterization is to clearly communicate the key findings of the assessment and to provide and clear and balances assessment of the strengths and limitations of the process. Risk characterization involves both scientific and policy based decision making, thereby resulting in a decision making process that blends both elements.

Sources of Uncertainty in Human Health Risk Assessment

Generating a list of the various sources of uncertainties that affect a human health risk assessment is the first step en route to understanding the results of the assessment. Such a list will help structure the analysis and ensure that major sources of uncertainty are identified. In this section, common sources of uncertainty in human health risk assessments are described and classified according to type of uncertainty.

There are many sources of uncertainty in a typical risk assessment. In a human health risk assessment, we may be uncertain about the identity of the sub population at highest risk of exposure, routes of exposure, intake rates, concentrations in different media, sensitivity of different age groups to the chemical of interest, importance of modifying factors (*e.g.*, diet, health), *etc*. Despite the long list of possible sources of uncertainty, they all belong to one of four general types of uncertainty: variability, and incertitude arising from lack of knowledge about parameter values, model structure, and decision rules. For a more in-depth discussion of these types of uncertainty, Finkel (1990).

Variability refers to observed differences in a population or parameter attributable to true heterogeneity (Warren-Hicks and Moore, 1998; U.S. EPA, 1999). It is the result of natural random or stochastic processes and stems from, for example, environmental, lifestyle and genetic differences. Examples include variation between individuals in size (*e.g.*, height, weight) and physiology (*e.g.*, metabolic rate, food intake rate), and between environments (*e.g.*, soil type, climate, chemical concentration).

Parameter uncertainty refers to our incertitude about the true values of the parameters or variables in a model (Warren-Hicks and Moore, 1998; U.S. EPA, 1999). Parameters are often estimated from laboratory, field or other studies. This type of uncertainty is introduced because the estimated value typically relies on insufficient, unreliable or partially relevant information for the parameter of interest. Several processes contribute to parameter uncertainty including measurement errors, random errors, and systematic errors (Finkel, 1990). Measurement error often arises from the imprecision of analytical devices used, for example, to quantify chemical levels in different media or measure levels of detoxifying enzymes in humans. Errors in measurement, however, are not necessarily restricted to analytical hardware. Reconstructing past releases at a contaminated site may be subject to measurement error because historical data can

be faulty or ambiguous. Random error or sampling error is a common source of incertitude in human health risk assessment and arises when one tries to draw an inference about a quantity from a limited number of observations.

In risk assessment, we use mathematical models to determine which variables to measure, specify how they relate, and to estimate the values of variables we cannot measure directly. Model uncertainty is a serious challenge in risk assessment (Finkel, 1990; Reckhow, 1994). Different dose-response models, for example, commonly lead to two-fold or more differences in estimated low toxic effects doses (*e.g*., ED5 or LD10), even when the list of models is restricted to those that fit the data equally well and are theoretically plausible (Moore and Caux, 1997). The problem of model uncertainty is likely to be much more serious with complex models such as regional-scale fate and transport models. Most applications of uncertainty analysis in human health risk assessment do not propagate uncertainties associated with model structure, rather the model structure is assumed reasonable and only parameter uncertainties are propagated.

Decision rule uncertainty comes into play during risk management, *i.e*., after a risk estimate has been generated. This type of uncertainty arises when social objectives, economic costs, value judgements, *etc*. are part of the decision-making process for deciding on what actions to take to remediate a problem. Individual decision makers are likely to be uncertain about how to best represent the complex preferences of their constituents. Such uncertainty can be quantified by collection of empirical data (*e.g*., opinion polls) and formally treated *via* decision analysis, but rarely is. Even with the availability of formal analytical tools, controversial judgments remain about how to value life, distribute costs, benefits and risks among individuals and groups, and deciding whether to reduce risks now or some time in the future (Finkel, 1990).

When assumptions need to be made during the risk assessment process, either because of data gaps or knowledge gaps and unknowns, each assumption results in some degree of uncertainty in the overall conclusions of the assessment. In order to understand the uncertainties within the HHRA and to ensure that the impact of these uncertainties is full understood, it is important to document and characterize each of these. To ensure that the risk assessment does not underestimate the potential for the occurrence of adverse effects, it is necessary to make assumptions which are conservative. In other words, assumptions are made that tend to overestimate exposure, toxicity and risk, rather than underestimate these parameters. The following sections describe areas of uncertainty within the current risk assessment, and discuss the potential impacts of these uncertainties on the conclusions drawn from the assessment. Given the tendency for the assumptions described below to overestimate both exposure and toxicity, it is considered extremely unlikely that the overall risk characterization resulted in underestimated potential health risks.

8.1 Uncertainties in the Exposure Assessment

The current exposure assessment has provided a range of potential exposures for each scenario. The range is described by three individual estimates of exposure, including a high, low and central estimate. The high-case estimate employs a series of individual worst-case assumptions, applied one after another, introducing a repetitive input parameter selection bias. The high-case estimates truly represent a worst-case scenario. Similarly, the central and low exposure estimates employed, whenever possible, central (average) and low-end exposure parameters, respectively. The upper and lower estimates of exposure represent the extreme boundaries of plausible exposures, while the central tendency represents the most likely case. A range of potential

exposure values (facilitated through the use of selected low, central and high input parameters) were developed to provide a general appreciation for the level of uncertainty and variability present within the quantitative exposure estimates.

The following represent a list of assumptions that were used during the development of exposure estimates:

- It was assumed that Canadian military personnel involved in the herbicide spraying would have varied from year to year;

- Contaminant levels were assumed for the actual herbicide product not the active ingredient.; for example in 1966 a 70:30 mix of 2,4-d and 2,4,5-T was applied, this product was assumed to have a similar TCDD content as Agent Orange; this TCDD content was applied to the whole mixture rather than only the 2,4,5-T portion.

- At the time of application, there was no discernible contamination of 2,4-D by PCDDs or PCDFs; however, since contaminants levels were assumed for the herbicide product not the active ingredients, this assumption will not impact the risk estimates.

- For central tendency estimates, it was assumed that the mixer/loader/applicator and flagger (PHED approach only) were wearing a single layer of clothing in addition to gloves during routine work. It is, of course, plausible that individuals may have been wearing more or less clothing throughout different times of the day;

- The influence of different liquid carries (*e.g.,* diesel *versus* water) on the dermal absorption kinetics of dioxins and HCB is uncertain and cannot be quantified. It was assumed that all mixtures containing dioxins and HCB would be absorbed by the skin in a similar manner;

- An accident scenario was assumed to occur once a day and involve direct dermal contact with a liquid herbicide mixture either as a result of a spill or direct spray event. The duration in which the liquid herbicide mixture (and hence the contaminant of concern) was assumed to be in contact with the skin was approximately 20 minutes. The proportion of the applied dermal dose which is absorbed is a function of the amount of time a liquid is in contact with the skin;

- The accident scenarios evaluated are considered extreme cases; however, it is unknown whether these types of incidental exposures actually occurred during the 1966/67 trials. In the absence of any information to suggest otherwise, it is only reasonable to assume these types of accidental spills and/or spray events occurred. It is recognized that the exposure estimates resulting from the two accident scenarios are significantly greater from those generated using the PHED approach. Although it has been suggested that the PHED approach inherently accounts for accidental exposures, the details with respect to this methodology are not known..

- Although it is generally understood that the forest canopy would intercept a significant proportion of the intended herbicide application rate, no site-specific data on canopy intercept fractions were available. A range of canopy intercept fractions were employed. As previously discussed, the most likely canopy intercept fraction was considered to be approximately 90%; and,

- The exposure scenarios developed here are based on a reconstruction of historical events and, therefore, the degree of uncertainty associated with typical operational practices at the time (*e.g.*, the use of personal protective equipment, the manner in which herbicide products were handled and transported, *etc*.) is considered high. As a result, a range of plausible exposure parameters (*e.g.*, amount of protective clothing worn, *etc*.) were used in attempt to capture these uncertainties.

8.2 Uncertainties in the Toxicological Assessment

The following conservative assumptions were used in development of toxicological criteria for the chemicals of potential concern in order to increase the confidence that potential risks would not be underestimated:

- TRVs utilized in the risk assessment are inherently conservative, as they are set at levels several fold lower than the lowest known effect level. This ensures that they are set at levels where there is a reasonably high degree of certainty that no effect would occur;

- HCB was treated as a genotoxic carcinogen utilizing the Health Canada cancer slope factor that assumes no threshold in the evaluation of carcinogenic risk. In fact, the carcinogenic mechanism of action for HCB is likely non-genotoxic and would have a dose-response threshold;

- For genotoxic carcinogens it was assumed that one mutation could produce cancer and that no repair of genetic lesions occurs. Therefore, this possible mechanism means that no threshold would exist for chemicals that produce self-replicating lesions. However, the existence of enzymes that routinely repair damage to DNA are well documented in the scientific literature, and the potential adverse effects arising from damage to DNA would only be observed if the ability of these repair enzymes to "fix" the damage was exceeded;

- Dioxin was assumed to act only *via* a threshold mechanism;

- The chronic TRV for dioxin is based on an endpoint of questionable relevance to the Tier 1 assessment; the endpoint relates to effects in the off-spring of exposed females, the relevance of which is questionable when considering military personnel in 1966-67 were likely predominantly male; that said, TRVs established by recognized regulatory agencies are not sex specific and it was beyond the scope of this assessment to develop a male specific TRV; if developed, male specific TRVs would be equally or less conservative than those utilized in this assessment;

- The acute TRV for dioxin, derived by ATSDR (1998) is based on immune suppression in mice exposed to dioxins which leads to an increased susceptibility to the influenza virus. ATSDR (1998) classifies this effect as "less serious" since it is reversible.
- Large safety factors (*i.e*., 100-fold or greater) were used in the estimation of the TRV for threshold-type chemicals. These safety factors were applied to exposure levels from studies where no adverse effects are observed (*i.e*., to the NOAEL). Thus, exceeding the toxicological criterion does not mean that adverse effects would occur, rather it means that the safety factor beyond the no-effect exposure is somewhat reduced;

- It was assumed that the half-life of dioxin-like compounds in humans was 7.1 years. There exist a range of half-lives reported in the literature of up to 8.9 years. Essentially all exposures for herbicides that contained 2,4,5-T (Agents Orange and Purple as well as other formulations that were prepared for some plots) were contaminated exclusively with TCDD and virtually no significant levels of other dioxin congeners. As discussed in the toxicological profile the response to acute exposure to TCDD in humans is sequestration in the liver and an initial phase of rapid elimination; this suggests that the assumption of a constant half-life for large exposures to TCDD is overly conservative;

- Pentachlorophenol (PCP) was applied to two test plots during the 1967 trials. Use of PCP introduces a wide range of dioxin congeners that are not associated with 2,4,5-T or the other herbicide products used during the 1966 and 1967 trials. However, because PCB was only applied to two plots this was not considered a significant concern.

- Humans were assumed to be the most sensitive species with respect to toxic effects of chemical. However, for obvious reasons, toxicity assays are not generally conducted on humans, so toxicological data from the most sensitive laboratory species were used in the estimation of toxicological criteria for humans. Because some evidence indicates that the laboratory species used to establish TRV are more sensitive than humans to the toxic effects of dioxins, the potential impacts on humans would be less than indicated by the laboratory information;

- The most sensitive toxicological endpoint (for example decreased growth, body weight loss/gain, reproductive effects) was selected for each chemical from the available scientific literature to represent the exposure limit; and,

- The rate of elimination of TCDD in response to acute, high level exposures to humans after industrial accidents or after accidental oral ingestion has been described by Bertazzi *et al*., 2001 and Geusau *et al.,* 2002 (discussed in detail Appendix A). Recent studies that have measured TCDD blood concentrations shortly after high-level exposure to TCDD indicate that the half-life in the human body is dose dependent (Geusau *et al.,* 2002). Similar findings have been reported for the Ranch Hand cohort (Michalek *et al.,* 2002). In the opinion of Emond *et al.* (2005; 2006) the use of first-order elimination of TCDD to estimate past exposures to TCDD, especially those that occurred over a short duration and involved relatively large concentrations might underestimate actual exposures. In other words, the body burden determined today may actually be much lower than would be predicted by the linear half-life model. Thus, the variability introduced by exposure-dependent induction of CYP1A2 and an initial rapid elimination of TCDD may suggest

the predicted chronic body-burden for dioxin described in this report is overly conservative.

8.3 Uncertainties in the Risk Characterization

- The one-hit cancer model advocates the potential for an elevated cancer risk following a singe dose exposure. This model could only be relevant for potent genotoxic carcinogens where the genetic lesions they produce could not be repaired. It is highly unlikely that HCB would act in this manner (as discussed above, the carcinogenic mechanism of action for HCB is likely non-genotoxic and threshold based; and,

- It is uncertain as to whether or not an adverse health effect would exist among receptors with a chronic dioxin body burden greater than the 27.8 pg TEQ/g lipid. The body burden level of 27.8 pg TEQ/g lipid was calculated using an exposure rate which was equivalent to the chronic TRV for dioxin of 2 pg TEQ/kg bw/day. As previously discussed, this chronic TRV was designed to be protection of reproductive effects in subsequent generations of off-spring.

- For the purpose of estimating HCB related cancer risks, a duration of exposure of one year has been assumed even though these exposures occurred over a 3 or 4 day time span. This likely overestimates HCB related cancer risks.

9.0 CONCLUSIONS AND DISCUSSION

Dioxins

- With the exception of the Applicator scenario, the short-term risk estimates for all acute exposure scenarios (under the central exposure estimate) were greater than a HQ value of 1.0, indicating that the central exposure estimates exceeded the short-term or acute TRV (200 pg TEQ/kg bw/day). A HQ value greater than 1.0 does not indicate that adverse health effects would have occurred; however, it does indicate that some receptors may have experienced elevated exposures and as such, the potential for elevated risks.

- With the exception of two accident scenarios (for the Mixer/Loader spill scenario and the Flagger/Trainee spray scenario), the short-term risks predicted through this evaluation have been classified as "less serious". "Serious" effects were not noted until exposures of more than 300-fold greater than the acute TRV. These "less serious" exposure levels are not indicative of elevated risks of long-term irreversible health effects, rather, the potential for short-term reversible effects, of the nature considered "less serious".

- Risk estimates predicted for the accident scenarios are indicative of potentially 'serious' effects; however, the occurrence of accidents of this nature during the 1966 and 1967 spray periods remains uncertain. While elevated risks do not necessarily equate to certain effects it does raise the level of concern and indicates that further epidemiological investigation of individuals involved in these operations is warranted.

- Long-term or chronic risk estimates for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas more than a year following the spray applications are all less than levels that would be indicative of a concern (HQ < 1); as a result, no dioxin related adverse health risks are predicted for military trainees potentially exposed in this manner.

- Elevated body burden were predicted for the two accident scenarios. Elevated body burdens (*i.e.,* levels above the Body Burden $_{TRV}$) may have persisted in persons experiencing accidental exposures for approximately 52 years following the initial accidental spray/spill event. Background individuals (*i.e.,* those not involved in spraying activities at CFB Gagetown) of the same age were predicted to have dioxin body burden levels above the Body Burden$_{TRV}$ for 17.5 years. In other words, dioxin body burden levels among the general population in the 1960's and 1970's were greater than the levels considered acceptable today.

- The body burden results of this assessment are comparable to estimates for the Ranch Hand Veterans who served in Vietnam.

- Based on this assessment, the current body burden levels of individuals who may have experienced elevated exposures during the 1966/67 trials would not likely be distinguishable from the body burden levels of the general population. Although these individuals may currently have body burden levels similar to those of the general population, these individual likely experienced many years of elevated dioxin body burden levels relative to the general population.

- Further investigations of individuals who were present in the vicinity of the spray applications during 1966 and 1967, and may have been experienced these acute exposure events though accidents similar to those considered herein, is warranted. These further investigations could involve body burden analysis, although as indicated above, 40 years after these exposures the body burdens of people are not likely to be distinguishable from the body burden levels of the general population. Additionally, this further investigation could involve an epidemiological study of exposed individuals wherein the incidence of health effects related to the chemicals of concern is investigated.

Hexachlorobenzene

- Short-term or acute estimates for all acute exposure scenarios, with the exception of the mixer/loader accident scenario, are less than levels that would be indicative of a concern (HQ < 1). HQ estimates marginally exceed the 1.0 benchmark for the high end (worst case) mixer/loader accident scenario only. This exposure scenario is considered highly conservative. Given the marginal exceedances estimated and the highly conservative nature of this evaluation, these exceedances are not considered significant or indicative of a potential health risk.

- Long-term or chronic risk estimates for military trainees who may have inadvertently trained in either the 1966 or 1967 spray areas more than a year following the spray applications are all less than levels that are indicative of a concern (HQ < 1 and ILCR < 10^{-5} or 1/100,000); as a result, no HCB related adverse health risks are predicted for military trainees potentially exposed in this manner.

- Lifetime cancer risk estimates for all acute exposure scenarios, with the exception of the mixer/loader accident scenario, are less than levels that are indicative of a concern (ILCR < 10^{-5} or 1/100,000). ILCR estimates marginally exceed the 10^{-5} benchmark for the high end (worst case) mixer/loader accident scenario. ILCR estimates for the central tendency receptor are essential equivalent to the benchmark for the 1967 spray period. These risk estimates assume the potential for an increased cancer risk following a one-hit exposure. The evaluation of cancer risks following acute duration exposures is an area of high uncertainty and questionable relevance. Given the marginal exceedances estimated and the highly conservative nature of this evaluation, these exceedances are not considered significant or indicative of an elevated cancer risk.

10.0 DOCUMENT SIGN-OFF

The risk assessment has been performed in accordance with accepted practice and usual standards of thoroughness and competence for the profession of toxicology and environmental risk assessment. The information, opinions and recommendations provided within the aforementioned report have been developed using reasonable and responsible practices, and the report was completed to the best of our knowledge and ability. Any information or facts provided by others, and referred to or utilized in the preparation of this report, is believed to be accurate without any independent verification or confirmation by CEI. This report is based upon and limited by circumstances and conditions stated herein, and upon information available at the time of the preparation of the report.

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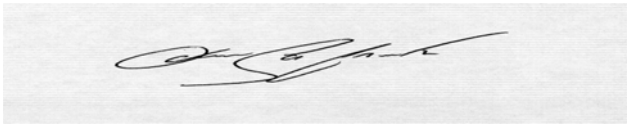

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