8 UNCERTAINTY ANALYSIS

Uncertainty is inherent in any risk assessment process even when using the most accurate data and sophisticated models because risk assessment is a complex process requiring the integration of multiple phases ranging from release of chemicals in the environment to the estimation of dose and potential of adverse health effects in the human population. As discussed in Sections 1.9 and 1.10 of this MPHRA report, CDPHE and USEPA guidance and policy were used to establish the risk assessment process. As suggested by those guidance and policy documents,, this first tier screening-level MPHRA was performed to obtain a reasonable maximum estimate of risk; therefore reasonably conservative values and assumptions were utilized to calculate the risk for a hypothetical RME individual.. Nonetheless, even with the high level of conservatism incorporated into these screening-level MPHRA calculations, uncertainty exists when evaluating the potential health impacts of a process, especially those as complex as the PCAPP and EDS processes. As discussed throughout this report, a large quantity of data sources and algorithms constitute the PCAPP and EDS MPHRA model. The MPHRA model requires integration of multiple physical and chemical parameters, ranging from release of chemicals into the environment to the estimation of dose and potential of adverse health effects in the human population, which is highly variable due to differences in age, genetics, lifestyle, and activity levels. Definition of these parameters to assess risks to humans is frequently limited by a lack of knowledge regarding a number of these factors, thus leading to some degree of uncertainty when interpreting results.

Table 8-1 lists categories of uncertainty that may impact the MPHRA results. Table 8-1 also summarizes the risk assessment procedures or data inputs used in each category of uncertainty. The potential impact of these sources of uncertainty were either qualitatively evaluated or quantitatively estimated. Generally, the majority of sources of uncertainty in a risk assessment can be identified qualitatively but not quantified because of the lack of supporting data. Uncertainty that may be attributable to a process that is poorly understood cannot be quantified with any confidence.

Table 8-1. MPHRA Uncertainty Categories

Uncertainty Category	Source of Uncertainty	Risk Evaluation Method
Facility Characterization (see Section 2)	• Operating requirements • Expected COPC identification • COPC emission rates	• Use engineering design • Utilize mustard research documentation • Apply specific test data • Evaluate alternative emission scenarios
Exposure Assessment *Exposure Parameters* (see Section 4)	• Exposure pathways • Food/water ingestion rates • Body weight • Frequency and duration of human activity • Lifetime duration	• Identify potential pathways • Incorporate RME (screening-level) assumptions
Exposure Assessment *Exposure Point Concentrations* (see Sections 3 and 5)	• RME location • Average annual air concentration • Media concentrations • Meteorological parameters • Animal COPC uptakes • Human COPC uptakes	• Incorporate RME assumptions for screening-level risk assessment • Use fate, transport and uptake models to estimate concentrations in the media and food products for COPCs, per USEPA guidance and/or CDPHE policy
Toxicity Assessment (see Section 6)	• USEPA toxicity values • Alternate toxicity values from other agencies • COPCs with no toxicity values • Multiple chemical interactions	• Employ USEPA recommended toxicity value hierarchy • Apply route-to-route extrapolation • Evaluate alternative toxicity values • Evaluate interaction of multiple chemicals based on EPA guidance (assumption of additivity).

While Table 8-1 lists many categories of uncertainty, the MPHRA results presented earlier in Section 7 and summarized below, illustrate that although many sources of uncertainty may exist, uncertainty related to these few COPCs and pathways are most likely to impact the MPHRA results.

The cancer risk estimate is driven by:

- fish consumption pathway (65 percent of the total lifetime risk)
- breast milk consumption pathway (20 percent)
- inhalation pathway (7 percent)
- four COPCs drive over 99 percent of the cancer risk.

Chronic noncancer hazard, or HI is driven by:

- produce consumption pathway (59 percent of the HI)
- inhalation pathway (22 percent)
- breast milk pathway (17 percent)
- eight COPCs drive over 98 percent the noncancer hazard.

Acute noncancer hazard assessment evaluates only the inhalation pathway over a 1-hour averaging time.

- Five inorganic COPCs and HD drive the contribution to the worker acute hazard, producing over 95 percent of the acute HI.
- Three COPCs contribute 80 percent of the off-site acute HI.

Table 8-2 lists the specific sources of uncertainty that were identified and evaluated. Many were qualitatively evaluated in this MPHRA and found to be minor, producing little or no impact on MPHRA results. If sufficient data exists regarding experimental or measurement error/uncertainty, quantitative uncertainty may be assessed for a given result. Table 8-2 also provides a summary of the qualitative impact (i.e., potential under- and/or overestimation of result) from the sources of uncertainty and identifies those for which a quantitative evaluation was conducted. Many of the variables whose uncertainty could not be quantified are related to either COPC emission rates or COPC toxicity.

Table 8-2. Summary of Principal Sources of Uncertainty and their Potential Impacts on Calculated Risk and Hazard

Source of Uncertainty	Reason for Uncertainty	Direction of Uncertainty[a]	
		Over	Under
FACILITY CHARACTERIZATION			
Less than full time AFA stack emission	The COPC emission rates from the PCAPP stacks were based on design rate operations 24 hours per day, 7 days per week, 365 days per year, over a 5-year period without consideration for facility or equipment availability. At this processing rate, the PCD HD stockpile would be completely destroyed in 289 days.	X	
Less than 12 hours per day emission of HD from EDS	Each of two EDS stacks were assumed to emit HD continuously at 0.7 times the VSL of 0.003 mg/m^3 for 12 hours per day, yet processing in the EDS will require only a 1 hour emission release per day.	X	
Use of VSL as HD emission rate	Emission calculations used 0.7 times the HD VSL of 0.003 mg/m^3 to obtain emission rates for the AFA stack and the EDS stacks. However, the detailed emission calculations (see Appendix B) also present a more realistic HD emission estimates that are 50 times lower for the AFA stack and 1,000 times lower for the EDS stacks.	X	
Bulk oxidizer	Emission estimates for organic COPCs other than HD take no credit for additional emissions control by the Bulk Oxidizer.	X	
Use of controlled emission rates	The baseline MPHRA risk and hazard were calculated using COPC emission rates based on control efficiencies derived from vendor-supplied carbon control factors for 32 of the 69 organic COPCs with quantifiable emission rates. Emission rates for the remaining 37 organic COPCs were calculated assuming no control in the activated carbon. Actual removal efficiencies may result in higher emission rates for some of the 32 COPCs with applied control efficiencies and lower emission rates for the 37 COPCs with no applied control efficiencies. **Evaluated quantitatively (see Table 8-3).**	X	X
1,2-dichloroethane emission rate	Uncertainty exists in the 1,2-dichloroethane concentration in the HD feed, which could result in a 1,2-dichloroethane emission rate up to two times higher than that used in the baseline MPHRA. **Evaluated quantitatively (see Table 8-3).**		X
Metal and salt compounds	Metal and salt compounds are not expected to volatilize to any process gas stream and/or are expected to be controlled by pollution control equipment.		X
COPCs without emission rates	Twenty five (25) COPCs were identified that had insufficient data to estimate emissions (from both PCAPP and EDS); therefore, risk from these COPCs cannot be quantified. These COPCs were primarily identified in literature sources as mustard impurities and treatment and degradation products. Missing emissions data represents an underestimation of risk.		X
EXPOSURE ASSESSMENT			
COPC selection process	The COPC selection process used at this stage may result in over- or underestimation of risk. For example, chemicals identified in literature as mustard impurities and treatment and degradation products were eliminated from further consideration in the MPHRA if they were not detected in testing of processes similar to PCAPP (such as those at the Aberdeen Chemical Agent Disposal Facility). However, the selected COPCs will be refined once actual emission data are available.	X	X
Models used to estimate media concentrations	Various uptake and fate/transport models are used to estimate concentration of COPCs in the environment and ingestion media. The AERMOD regulatory fate and transport model applies conservative assumptions and parameters, and results of the modeling may be further conserved via user input and model analytic options. Combined uptake and fate/transport modeling may result in under- or overestimation of risk.	X	X
Default values for exposure parameters	Default values are used for various exposure parameters (e.g., body weight, exposure duration, exposure frequency, averaging time, ingestion rates for soil, water, and produce). . Typically, the default values are likely to overestimate risk but may result in under-estimation of risk in some cases. Please note that the degree of underestimation is not expected to be considerable in most cases.	X	X
Exposure via breast milk	Several input parameters for the model including biological transfer factors and half-life of chemicals in the body needed to estimate the concentration of chemicals in the breast milk are not available for COPCs identified for the breast milk pathway. The assumptions based on the limited available information in the literature could result in over- or under-estimation of risk.	X	X

Table 8-2. Summary of Principal Sources of Uncertainty and their Potential Impacts on Calculated Risk and Hazard (continued)

Source of Uncertainty	Reason for Uncertainty	Direction of Uncertainty[a]	
		Over	Under
Breast milk partitioning data	Breast milk partitioning coefficients needed for the breast milk pathway are not available for all COPCs identified in open literature. The assumptions used in this assessment could result in over- or underestimation of risk for non-lipophilic COPCs (i.e., COPCs which do not have tendency to accumulate in the fat tissue); no lipophilic COPCs are included in the assessment. **Evaluated quantitatively (see Table 8-3).**	X	X
Lifetime duration	The baseline cancer risk was averaged over a 78 year lifetime, as defined in the latest Exposure Factors Handbook (USEPA, 2011). However, at the request of CDPHE, an alternative USEPA default value of 70 year lifetime was evaluated in the uncertainty analysis as the averaging time for carcinogenic effects. Reduction of lifetime produces a corresponding increase in cancer risk. **Evaluated quantitatively (see Table 8-3).**		X
TOXICITY ASSESSMENT			
Chronic toxicity values	The risk assessment used RfC and RfD values to evaluate noncancer hazards and IUR and CSF values to quantify cancer risk. In many cases, these values are derived from a limited toxicity database, which can result in quantitative or qualitative uncertainty. To account for these and other uncertainties associated with the evaluation of toxicity data, USEPA conservatively derives both noncancer and cancer toxicity values. Toxicity values can result in over- or underestimation of risk.	X	X
Acute Toxicity Values	Acute toxicity values based on 1-hour exposure duration for the acute risk evaluation are available for a limited number of chemicals. The use of alternate sources and approaches for acute toxicity values for several COPCs is likely to result in over- or under-estimation of risk.	X	X
Route-to-route extrapolation of toxicity data for the report	Thirty five (35) COPCs are missing toxicity values for one, but not both, of the exposure routes (inhalation and oral) and were assigned an extrapolated toxicity value. This extrapolation was performed for cancer toxicity values (unless available data indicated the COPC is not a carcinogen via that route) and noncancer toxicity values. Route-to-route extrapolation was applied to only four carcinogenic COPCs, and none of these are in the list of top four COPCs (those contributing to 99% of the risk). Route-to-route extrapolation was applied to 35 non-carcinogenic COPCs, including five of the top 10 COPCs (those contributing 98% of the HI). Extrapolation can result in either an over- or underestimation of risk.	X	X
Toxicity values for HD	The currently available USCHPPM Army RfD is used to calculate noncancer hazard due to ingestion and is derived from the lowest-observed-adverse-effect-level (LOAEL) in animal studies with the highest total uncertainty factor of 3,000, resulting in an RfD that indicates a high level of uncertainty that might be overprotective or underprotective for noncancer health effects (NRC, 2000). The currently available USCHPPM Army RfC is used in the baseline assessment to calculate noncancer hazard due to inhalation and is derived from one human study and two animal studies with adjustments for exposure time and various uncertainties (CDC, 2004). Use of another RfC would either raise or lower the calculated hazard, depending on the magnitude of the alternate value. The CSF is used to calculate cancer risk due to ingestion. The CSFs derived by various researchers (seven studies total) ranged from 1.6 to 95, with the geometric mean being 7.7. The mean CSF, the value chosen for use by USAPHC, is used in the baseline assessment. Use of the maximum CSF results in an increase in cancer risk. **Evaluated quantitatively (see Table 8-3).** The IUR is used to calculate cancer risk due to inhalation. The IUR used in this MPHRA is the US Army's recommended IUR for HD. Use of the USEPA IUR results in an increase in cancer risk. **Evaluated quantitatively (see Table 8-3).**	X	X

Table 8-2. Summary of Principal Sources of Uncertainty and their Potential Impacts on Calculated Risk and Hazard (continued)

Source of Uncertainty	Reason for Uncertainty	Direction of Uncertainty[a]	
		Over	Under
Agents T and HT toxicity	This risk assessment assumes that all agent contained in the munitions to be treated at PCD is HD. The agent within the 155-mm and 105-mm projectiles is comprised entirely of HD. However, 21 percent of the 4.2-inch mortar rounds are comprised of HT (a mixture that contains approximately 60 percent HD and 40 percent Agent T). The HT contained within this portion of the 4.2-inch mortar rounds represents 2.3 percent of the total weight of the agent stockpile. No specific toxicity data exist for HT. The CDC maintains that HD and HT are chemically and toxicologically related and can be described by HD alone (CDC, 2003). CDPHE disagrees with this assessment maintaining that the limited toxicological studies available suggest T may have increased toxicity as compared to HD. Therefore, this risk assessment may over- or underestimate risk by assuming that all agent is HD, including the 2.3 percent of the agent stockpile that is HT.		X
COPCs with no toxicity values	Twenty eight (28) COPCs that may potentially be present in PCAPP or EDS emissions lack chronic toxicity values available for the sources listed in the hierarchy in Section 6.1, for any mode of action and cannot be considered in the chronic risk and hazard calculations. Fifteen (15) COPCs have no verified acute toxicity values and cannot be considered in the acute hazard calculations, nor can they be included in a route-to-route extrapolation. Lack of toxicity values for these COPCs represents an underestimation of risk and hazard.		X
Hierarchy for toxicity value selection	The toxicity values used in this assessment were obtained based on the hierarchy recommended by USEPA. However, use of this hierarchy may not yield the most conservative of the available toxicity values.		X
Interaction of multiple COPCs	While it is recognized that both synergistic and antagonistic interactions are possible between COPCs, this MPHRA follows USEPA guidance for chemical mixtures in assuming that carcinogenic risks and noncancer hazards from each COPC are additive. The presence of synergistic or antagonistic effects results in either under- or overestimation of carcinogenic risk or noncancer hazard.	X	X

a. Direction of uncertainty refers to whether the listed parameter causes the MPHRA to overestimate (over) or underestimate (under) the risk or hazard.

8.1 QUANTITATIVE EVALUATION OF UNCERTAINTIES

Several sources of uncertainty identified in Table 8-1 and Table 8-2 also were evaluated quantitatively as follow. Because these sources of uncertainty have a range of potential values, it may be appropriate to use the most conservative value, in addition to the screening-level value, to obtain a range of results that bound the upper- end of the estimated risk and hazard. In general, the factors evaluated quantitatively were related to the PCAPP and EDS process designs and COPC toxicity. Table 8-3 summarizes the results of the quantitative evaluation for those factors.

8.1.1 Use of Controlled Emission Rates

Uncertainty in COPC emission rates, as noted in Section 2, relates to the engineering design basis that includes the use of activated carbon for control of 32 of the 69 organic COPCs with quantifiable emission rates. The baseline MPHRA risk and hazard were calculated using emission rates based on activated carbon control factors obtained from an activated carbon vendor. This results in various degrees of organic COPC reduction from PCAPP and EDS processes, as indicated in Tables 2-2 and 2-3. For both the chronic and acute quantitative uncertainty assessments, the carbon control efficiency was reduced to zero for the 32 organic COPCs with control efficiencies greater than zero. Table 8-3 summarizes the results of this evaluation.

To fully appreciate the impact of this uncertainty evaluation, an important pattern to the risk results should be recognized. Only four COPCs account for 99 percent of the baseline cancer risk, and the emission rates for three of them were already based on no control in the activated carbon (i.e., 0 percent carbon control was assumed). The emission rate for the fourth (HD) was based on 0.7 times the HD VSL (i.e., not based on a carbon control factor). Therefore, the risk presented by these top risk-driving COPCs will not change when a different assumed activated carbon control efficiency is evaluated in the quantitative uncertainty assessment. Similarly for the hazard results, only eight COPCs account for over 98 percent of the baseline noncancer hazard, and only one of their emission rates (that for thiodiglycol) was calculated using an assumed baseline carbon control efficiency (66 percent). Baseline emission rates for the other seven COPCs that drive the baseline hazard were based on no control in the activated carbon control system.

8.1.2 Emission Rate for 1,2-dichloroethane

A propagation of error analysis of DOT headspace sampling determined that the concentration of 1,2-dichloroethane in the HD feed could be up to 134% higher than what was reported. This adjustment was applied to the calculated concentration of 1,2-dichloroethane in agent, and emissions were recalculated accordingly. The resulting higher emission rates were used in the chronic and acute uncertainty assessments.

8.1.3 COPC Partitioning Data for Breast Milk Exposure Pathway

Some toxicity- or exposure-related values can also be assessed quantitatively. One such value is related to the breast milk pathway (previously identified as an important pathway for this MPHRA). USEPA guidance indicates that approximately 90 percent or greater of a mother's intake of lipophilic (fat-soluble) chemicals is partitioned into the fat and the remainder into the blood (USEPA, 1998). Inorganic and organic compounds of metals are found in human breast milk, but are not associated with milk fat. Limited data exist on the relative distribution of these more water soluble (non-lipophilic) chemicals between phases in human milk. Therefore, in the absence of specific values for COPC partitioning into breast milk components, mid-point COPC-

specific partitioning values were selected for the baseline MPHRA. This assumption could result in over- or underestimation of risk for non-lipophilic COPCs (i.e., COPCs which do not have tendency to accumulate in the fat tissue).. Because the breast milk pathway is one of the major contributors to risk and the COPCs identified for this screening-level risk assessment are not considered lipophilic (i.e., do not accumulate in fat), the most conservative COPC-partitioning values were selected for the quantitative uncertainty assessment by assuming that 100% of mother's chemical intake is partitioned into the blood.

8.1.4 Lifetime Duration

The baseline cancer risk was averaged over a 78 year lifetime, as defined in the latest Exposure Factors Handbook (USEPA, 2011). However, at the request of CDPHE, an alternative USEPA default value of 70 year lifetime was evaluated quantitatively in the uncertainty analysis, as the averaging time for carcinogenic effects. Reduction of lifetime produces a corresponding increase in cancer risk.

8.1.5 Cancer Toxicity Values for HD

Uncertainty associated with other HD toxicity values was evaluated quantitatively. Alternative values for chronic exposures to HD were evaluated in the uncertainty analysis. This MPHRA used a CSF for HD derived by the USAPHC (USAPHC, 2011b) of 7.7 per mg/kg of body weight-day, which is the geometric mean of the slope factors estimated using seven different data sets/methods (slope factors of 1.6, 5.0, 2.6, 5.3, 15.6, 9.5, and 95 per mg/kg of body weight-day). In the derivation of this CSF, USACHPPM noted that these seven values are distributed log normally and:

> "[T]herefore, the geometric mean of 7.7 per mg/kg-day is considered to be the best overall measure of the slope factor for HD. It should be noted, however, that the slope factor of 95 per mg/kg-day could be considered an outlier in the available data set (D. Gaylor, FDA, personal communication to A. Watson, ORNL, 9 June, 1998). If this value is not used in the calculation, the final geometric mean based on the remaining six values would be 5.0 per mg/kg-day."

Nonetheless, USACHPPM chose to include the slope factor of 95 per mg/kg of body weight-day in their approved oral CSF for HD (USACHPPM, 1999). Therefore, the oral CSF of 7.7 per mg/kg of body weight-day was used in the MPHRA. At the request of CDPHE, the USEPA recommended oral CSF of 95 per mg/kg of body weight-day was also quantitatively evaluated as an alternative maximum value in the uncertainty analysis.

The IUR for HD used to estimate the risk due to inhalation of HD presented in Section 6.1 is the US Army's recommended IUR for HD of 0.0041 per $\mu g/m^3$, which is based on the geometric mean of the various IURs reported by researchers and summarized by USACHPPM (USACHPPM, 2000). However, the USEPA recommends the use of an IUR of 0.085 per $\mu g/m^3$ (USEPA, 1991). In the 1991 basis for its inhalation IUR, USEPA noted that

> "[t]he dose-response estimates are considered to be highly uncertain, but to a degree that could not be measured. The McNamara et al. (1975) study was not of a standard design, and the assumptions required to do a quantitative analysis are considered to be relatively tenuous...too few animals were exposed and followed for a lifetime to give adequate sensitivity for detecting long-term effects, and the uncertainty about the experimental concentrations is too great to allow confidence about the absolute potency value."

Therefore, the US Army considers the use of the USACHPPM IUR for HD as appropriate for the MPHRA given the uncertainty of the USEPA IUR, as demonstrated by the range of reported values. Nonetheless, the USEPA IUR for HD was evaluated in the uncertainty analysis.

Table 8-3. Summary of Quantitative Estimation of Uncertainty to Calculate Probable Range of Risk and Hazard

Variable	Baseline Parameter and Risk Estimate Value	Alternative Parameter and Risk Estimate Value with Uncertainty
PCAPP 1,2-dichloroethane emission rate (lb/hr)		
AFA Stack	2.00×10^{-1}	3.70×10^{-1}
30-day Hydrolysate Storage Tanks Vent	4.77×10^{-4}	1.11×10^{-3}
BTS Stacks	2.06×10^{-1}	4.82×10^{-1}
BRS Stack	1.40×10^{-4}	3.28×10^{-4}
BC Feed Tanks Vent	3.37×10^{-7}	7.88×10^{-7}
Other PCAPP and EDS organic COPC emission rates	activated carbon control equal to 66%, 33%, or 0% (see Table 2-2 for long-term and Table 2-3 for short term)	activated carbon control equal to 0% for all COPCs (see page B-2-33 for EDS and B-1-25, B-1-28, B 1 29, B-1-32, and B-1-36 for PCAPP)
Fraction of COPC stored in maternal fat (dimensionless)	0.5	0
IUR for HD $(\mu g/m^3)^{-1}$	0.0041	0.085
Oral CSF for HD $(mg/kg\text{-}day)^{-1}$	7.7	95
Lifetime (years)	78	70
Quantifiable Uncertainty Impact on Risk Estimation Results [a, b, c, d]		
Lifetime cancer risk	0.27×10^{-6}	0.53×10^{-6}
Chronic (noncancer) HI	0.030	0.055
Acute worker HI	0.13	0.13
Acute residential HI	0.011	0.013

a. Reported values for the cancer risk and chronic HI are for the human receptor with the highest lifetime risk (one of the subsistence farmer or fisher receptors).
b. CDPHE acceptable risk = 1.00×10^{-6}.
c. CDPHE acceptable HI = 0.25.
d. CDPHE acceptable acute HI = 1.0.

8.2 SUMMARY OF UNCERTAINTY IN RISK CHARACTERIZATION

All the RME risk estimates in this evaluation are based on annual average air concentrations and reasonably conservative exposure assumptions and toxicity values. Therefore, the total estimated risk at the RME location is intended to be conservatively high, but specific COPCs and receptor combinations may individually under- or overestimate risk.
Some of the sources of uncertainty discussed herein produce a quantifiable effect, while the effect of others can only be assessed qualitatively. Table 8-2 presented an overview of the sources of uncertainty that were reviewed in both the quantitative and qualitative uncertainty analysis and included an indication as to whether the source potentially produces an overestimate, underestimate, or over-and underestimate of risk. Although some uncertainty exists that cannot be quantified in this MPHRA, the estimated baseline risks and hazards are , less than approximately one quarterof the CDPHE acceptable levels. From Table 8-3, when uncertainty that may underestimate risk is included for those variables/parameters for which uncertainty can be quantified, resulting risk and hazards remain no more than approximately one half of CDPHE acceptable levels.