REPORT ON PESTICIDE RAPID ASSESSMENTS

Minnesota Department of Health

MINNESOTA MDH DEPARTMENT OF HEALTH

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The Pesticide Rapid Assessment Project was made possible by funds from the Clean Water Fund, from the Clean Water, Land and Legacy Amendment.

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December 2014

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Executive Summary

The Minnesota Department of Health (MDH) Health Risk Assessment Unit developed a new, rapid way to assess health risks of chemicals in drinking water. Rapid assessments were completed for 159 pesticides selected by the Minnesota Department of Agriculture or Minnesota Department of Health. The chemicals were selected because no MDH drinking water guidance was available or the guidance was outdated.

The result of a rapid assessment is an amount of chemical in water that is unlikely to harm people who drink the water. MDH used information on toxic (harmful) effects of pesticides and risk assessment methods used by MDH for other types of drinking water guidance. The values that result from the rapid assessments are likely to be low compared to the result MDH would produce from an in-depth and lengthy review of the same chemical.

MDH recommends using the results of the rapid assessments to decide if a chemical found in water is present at a level that is low enough to cause no harm to people drinking the water. An important use of the rapid assessments is to provide the public with health-based information if their water is contaminated and no other standards or guidelines are available. If water analysis shows a chemical is present at a level higher than the assessment, additional research may be necessary to make decisions on cleaning up contaminated sites. The rapid assessments can also be used to set priorities for additional research on exposure and risks, including use as targets for developing laboratory analytical methods and setting cleanup goals.

Background

The Minnesota Department of Agriculture (MDA) has a long history of requesting risk assessment advice from the Minnesota Department of Health (MDH). MDA called to MDH's attention, in letters to MDH in October of 2012 and again in 2013 (letter to MDH, October 30, 2013), the potential need for updated MDH drinking water guidance values for a list of 162 chemicals, primarily pesticides. MDA asked to be consulted concerning priorities if MDH devotes effort to developing guidance for the chemicals on the list.

In recent years MDH adopted new, standard methods for developing health-based guidance for drinking water contaminants. MDA staff have closely followed MDH improvements in risk assessments and correctly noted that new assessments of the listed chemicals would likely be different than previous assessments. MDH decided that MDA needs were closely aligned with MDH resources and work directions. As a result, MDH assigned staff to develop a rapid and efficient way of assessing the set of chemicals using, to the extent practical, MDH standard methods for developing health-based guidance for drinking water.

MDH conducted the rapid assessment work between January 2013 and August 2014. MDA staff was informed of the approach MDH was taking and interim results throughout the process.

MDH decided to develop a rapid assessment approach due to the nature of the request. MDA requires guidance that allows the agency to screen results of soil and water analyses. That is, to determine whether the results of measuring many samples, each containing multiple contaminants, indicates that exposure to the soil or water is likely to pose a health risk. When risks are negligible, MDA does not need to conduct cleanup or establish other ways to control environmental levels. Guidance that is highly conservative (possibly over-protective) can be used to screen out findings that do not pose a risk so that MDA can focus on those chemicals that pose the greatest risks to health. MDA had already conducted a similar rapid assessment of many of the chemicals and had discussed how to combine existing toxicity data with newer risk assessment methods that include a variety of assumptions about duration of exposure, magnitude of exposure, doses used in animal studies, and toxic effects at different stages of life. Similarly, MDH needed a rapid approach to determine the relative importance of conducting in-depth reviews of the toxicity of the chemicals on the MDA list. MDH wished to understand the extent to which a new assessment of each of the chemicals would change the current understanding of potential risk. This evaluation of how an assessment would change required use of current MDH risk assessment methods in combination with a rapid evaluation of the toxicity data for each chemical.

MDH found the set of chemicals to be well suited for a rapid assessment. The chemicals included pesticides (comprising herbicides, insecticides, and fungicides), pesticide metabolites/degradation products, and other agricultural-related chemicals. Pesticides are a class of chemicals for which a greater than ordinary amount of toxicity information is known due to regulatory requirements for use. Sometimes the data base for a pesticide is outdated or limited in scope because the pesticide has not been in use and re-registered for use. But in general, toxicity information for the vast majority of the agricultural chemicals of interest to MDA would be easily found through the US Environmental Protection Agency (USEPA).

This report includes a description of the method that MDH developed for rapid assessments, the results of the assessments, and how to interpret and use the results of rapid assessments. This report also describes how rapid assessments can be used to help inform risk management decisions.

Methods for Conducting Rapid Assessments

Overview

A significant effort was made to develop methods that provided a consistent and repeatable way of conducting rapid assessments of toxicity information for large numbers of chemicals. Methods were selected so that rapid assessments yield adequate and appropriate public health protection that is consistent with current MDH practice and similar assessments.

Regarding chemical toxicity, the overall difference in the toxicity data for what MDH considers an in-depth, full review compared to the rapid assessment is that MDH did not conduct a careful search for multiple sources of toxicity data or a careful review of the toxicity studies that were selected, historically, by USEPA for pesticide registration and risk assessment. MDH used the most current USEPA information available without reviewing alternatives that USEPA or other authorities may (or may not) have considered.

Regarding risk assessment methods, the overall difference in methods and calculations for what MDH considers an in-depth, full review and the rapid assessment is that MDH combined a reference dose for a long-term exposure (chronic toxicity) with the short term drinking water intake for a life stage at which exposure was greatest (the intake rate for a bottle-fed infant) and the MDH default relative source contribution factor for short-term, infant exposure to nonvolatile chemicals. This is consistent with MDH practice because the reference dose for a properly conducted long-term exposure period (chronic toxicity) is assumed to be protective of every stage of life. However, MDH has found that historically, long-term toxicity studies typically do not include the high exposures and potential greater susceptibility of early life. In an in-depth chemical review MDH would review each life stage and corresponding exposure duration to carefully determine which set of exposures and studies protect every portion of the population. The rapid assessment methodology is an efficient way of ensuring that every portion of the population is protected. MDH recognizes that the rapid method likely yields a more conservative (protective) result than the result of an in-depth, full review. MDH did not alter the standard method for assessing risks from carcinogens and the result is not likely more conservative (protective) than the result of an in-depth, full review of a carcinogen.

Step 1: Identify the Most Recent Human Health Assessment

a) If USEPA had completed a 2013 Human Health Benchmark for Pesticides (HHBP), it was assumed this was the most recent USEPA assessment (U.S. EPA, 2013).

b) If a pesticide did not have an HHBP, the most recent USEPA assessment available was used, such as a Registration Eligibility Decision (RED), Interim Registration Eligibility Decision (IRED), and/or Tolerance Reassessment Eligibility Decision (TRED) (U.S. EPA, 2014a).

c) If a RED was not available, other sources for USEPA assessments were searched. These included IRIS (Integrated Risk Information System), (U.S. EPA, 2014b; USEPA Docket; U.S. EPA, 2014c), and the Federal Register (U.S. EPA, 2014d).

d) If a USEPA assessment was not available or did not fully describe the key studies several additional sources were searched. These sources included:

- ATSDR (Agency for Toxic Substances and Disease Registry) (ATSDR, 2014)
- HSDB (Hazardous Substances Data Bank) (HSDB, 2014)
- EFSA (European Food Safety Authority) (EFSA, 2014)
- USDHHS (U.S. Department of Health and Human Services) (USDHHS, 2014)
- FAO/WHO (Food and Agricultural Organization of the United Nations and the World Health Organization) (FAO, 2014) (WHO, 2014)
- Cal EPA (California Environmental Protection Agency) (CalEPA, 2014)
- IARC (International Agency for Research on Cancer) (IARC, 2014)
- EC (Environment Canada) (EC, 2014)
- HEAST (US EPA Health Effects Assessment Summary Tables) (HEAST, 1997)

In some cases, the rapid assessment was not carried out beyond step 1 because data were not available. In a larger number of cases, the rapid assessment was not carried out using chemical-specific data, but has recommended the result of the rapid assessment of a surrogate chemical.

Step 2: Determine the Point of Departure

Health effects from exposure to chemicals in drinking water are categorized in one of two ways: cancer or non-cancer. A point of departure (POD) is either a cancer slope factor (a measure of how potent the chemical is at causing cancer) or a dose associated with the non-cancer effect in a particular study.

a) Generally, the POD selected by USEPA for chronic (non-cancer) assessments was used as the basis of the MDH rapid assessment.

b) For the cancer rapid assessment, an oral cancer slope factor (also called a cancer potency) derived and recommended by USEPA was used as the POD. Cal EPA was used as a source of slope factor when a USEPA value was not available or a more current Cal EPA value was available, as in the case of Chorothalonil.

Step 3: Determine the Appropriate Uncertainty, Variability, and Dosimetric Factors

MDH used current methods of assigning adjustment factors to the POD from a study or to the overall database. As a result, MDH typically made some adjustment that had not been considered by USEPA. Details about standard uncertainty and variability factors are described in MDH, 2009 (SONAR 2008/2009).

a) Intraspecies Variability

The difference in how individuals respond to a toxic substance can range widely, but the standard approach is to use a 10-fold adjustment to reflect the variability within human populations. For each chemical a 10-fold uncertainty factor (UF) was used to account for intraspecies variation.

b) Interspecies Extrapolation and Dosimetric Adjustment Factor (DAF)

The difference in how animals and humans respond to a toxic substance can be separated into a difference in how

doses are absorbed, distributed, metabolized, and excreted (the pharmacokinetics) as well as a basic difference in the cells and tissues of the species (the pharmacodynamics). MDH accounts for the first difference by using a species specific dosimetric adjustment factor (DAF). Depending on the experimental conditions, the following animal-to-human DAFs were used in calculating the rapid assessment (MDH, 2012):

- Chronic mouse = 0.15, sub-chronic mouse = 0.14
- Chronic rat = 0.27, sub-chronic rat = 0.23
- Chronic dog = 0.63, sub-chronic dog = 0.42
- Chronic rabbit = 0.48, sub-chronic rabbit = 0.45

MDH accounts for the second difference by using a 3-fold animal-to-human UF for the potential for humans to be more sensitive to a chemical than the animals that were studied. The 3-fold UF was used to account for interspecies differences for any POD based on an animal study.

c) LOAEL to NOAEL extrapolation

If in the critical toxicity study from the most recent USEPA assessment, the no-observed-adverse-effect level (NOAEL) was not determined, a 3-fold or a 10-fold UF was used to adjust the dose lower, depending on the severity of the effects observed at the lowest-observed-adverse-effect level (LOAEL). For example, a 3-fold UF was used for Mesotrione because the low dose in an animal study showed a relatively mild effect of an amino acid in blood and discharge from the eye and a 10-fold UF was used for Aldrin because of liver toxicity at the LOAEL.

d) Sub-chronic to Chronic Extrapolation Uncertainty

A 10-fold UF was used when a long-term (chronic) study was not available or appropriate for developing a chronic toxicity POD. MDH considered a UF when USEPA based a chronic assessment on a 1-year dog study. Another example is a 10-fold UF used for DDD because the POD was from a 27-week rat toxicity study. Exceptions to adding a 10-fold sub-chronic to chronic UF include cases where the mechanism of action of the chemical was known and appropriate to any duration of exposure (that is, not likely to become more serious with a longer duration of testing). Examples of exclusion include the health endpoints acetylcholinesterase inhibition and developmental effects.

e) Database Uncertainty

A database UF (3-fold or 10-fold depending on, for example, the severity of health effects) was used for chemicals that lacked essential toxicity data. There were several reasons for adding a database UF to rapid assessments. These include the following:

1) Inadequate Reproductive or Developmental Toxicity Data: A UF (3- or 10-fold depending on severity of effects) was used in cases where the USEPA identified a reproductive or developmental study data gap. For example, USEPA used a 10-fold UF for Chlorsulfuron because of the lack of an acceptable reproduction study. A database UF was also used when either USEPA or MDH identified significant uncertainties in reproductive or developmental toxicity studies. For example, a 3-fold UF for Diazinon was used because of reported neurodevelopmental effects and delayed maturation of reproductive and immunologic systems.

2) Endocrine Disruption: MDH incorporated a 3-fold or 10-fold database UF (depending on severity) to account for endocrine disruption effects that occurred at doses lower than the POD. In some cases, this uncertainty was included in the USEPA uncertainty factor, and in other cases, MDH determined that a UF was appropriate based on

a review of the literature. An example of this is the rapid assessment for glyphosate in which a 3-fold UF was used because available toxicity studies suggest that it may interfere with normal endocrine system function at a level lower than the POD.

Step 4: Calculate the Reference Dose for Non-Cancer Health Effects

The reference dose (RfD) is a standard measure of non-cancer toxicity. The RfD was calculated using the dose-adjusted POD (that is, the DAF x POD) and UFs (total UF).

UFs were multiplied together to calculate a total UF. When two 3-fold UFs are multiplied the result is a 10-fold UF, as a 3-fold UF is considered a half log unit. The possible totals for UFs as practiced by MDH are 10, 30, 100, 300, 1000, and, typically, no more than 3000. All UFs for animal studies incorporate the 3-fold animal-to-human extrapolation UF and the 10-fold human variability factor (30-fold total).

$$\text{RfD (in mg/kd-d)} = \frac{\text{DAF adjusted POD}}{\text{Total Uncertainty Factor}}$$

Example: Diazinon RfD calculation for non-cancer, where the point of departure in a rat study was adjusted with the appropriate DAF and the UFs of 3 for animal to human uncertainty, 10 for human variability, and 3 for database uncertainty (total UF = 3x3x10 = 100).

$$\text{RfD} = \frac{(0.02 \text{ mg/kg/day} \times 0.23 \text{ DAF})}{100 \text{ UF}} = 0.000046 \text{ mg/kg/day}$$

Step 5: Derive the Non-Cancer Rapid Assessment

MDH's standard non-cancer assessment algorithm for calculating short-term guidance was used to ensure that the rapid assessments were protective of the most highly exposed life stage in the population. For all chemicals, MDH used a drinking water intake rate of 0.289 L/kg-d (for bottle-fed infants).

MDH uses a relative source contribution (RSC) in non-cancer assessments for all durations of exposure to account for exposures from sources other than drinking water (for examples, pesticides in food, soil, or in dust of homes). MDH used an RSC of 0.5 in all rapid assessments, which is the MDH default for short-term exposure to nonvolatile chemicals. The RSC is a fraction and has no units.

$$\text{Rapid Assessment Result (in ug/L)} = \frac{\text{RfD} \times \text{RSC} \times \text{unit conversion factor}}{\text{Intake rate for infants}}$$

Example: Diazinon calculation for non-cancer.

$$\text{Rapid Assessment Result} = \frac{0.000046 \text{ mg/kg/d} \times 0.5 \times 1000 \text{ ug/mg}}{0.289 \text{ L/kg-d (Infant intake rate)}} = 0.08 \text{ ug/L}$$

MDH has determined that the precision of calculations for health-based guidance are limited and MDH rounds the results to one significant digit.

Step 6: Derive the Cancer Rapid Assessment

For carcinogenic pesticides for which an oral cancer slope factor (SF) was available, rapid assessments were calculated using MDH's standard algorithm for linear carcinogens. MDH uses an incremental or additional cancer risk level of 1 in 100,000 (1E-5) and age-dependent adjustment factors (ADAFs) established by EPA (EPA supplemental guidance) that are used with corresponding age dependent intake rates and exposure durations (MDH, 2010).

Rapid Assessment Result (in ug/L) =

$$\frac{\text{Additional cancer risk level x unit conversion factor}}{[(SF \times ADAF \times IR \times D)_{<2} + (SF \times ADAF \times IR \times D)_{2 \text{ to } <16} + (SF \times ADAF \times IR \times D)_{16+}] / 70 \text{ years}}$$

An example cancer rapid assessment calculation for a chemical with a cancer slope factor of 16.0 per mg/kg-d, the standard ADAFs (unitless), intake rates (in L/kg-d), and durations of exposure (in years, with a 70 year lifetime denominator) is provided below:

Rapid Assessment Result =

$$\frac{(1E\text{-}5) \times (1000 \text{ ug/mg})}{[(16x10x0.137 \text{ L/kg-d } x2yr) + (16x3x0.047 \text{ L/kg-d } x\ 14yr) + (16x1x0.039 \text{ L/kg-d}x54 \text{ yr})]/70 \text{ yr}} = 0.006 \text{ ug/L}$$

MDH has determined that the precision of calculations for health-based guidance are limited and MDH rounds the results to one significant digit.

Step 7: Additional Literature Search

After a rapid assessment was completed, an additional literature search was conducted for toxicity data that could potentially change result of the assessment. The additional sources included, at a minimum, the California Department of Pesticide Regulation (CDPR) (CDPR, 2014) and PubMed (PubMed, 2014). These sources were searched for relevant toxicity data such as endocrine disruption effects, cancer slope factors, NOAEL/LOAELs, and any significant new findings on toxic effects. If relevant data were located, they were used in MDH algorithms to calculate the rapid assessment.

Results

List of chemicals

MDH began with a list of 162 chemicals (letter to MDH, October 30, 2013). MDH removed from consideration four duplicates (metasulfuon-methyl, 2(2 methyl-4-chlorophenoxy), parathion-methyl, and 2,4,5-T) and 17 pesticides that had been assessed by MDH since 2008 using current methods and assumptions or for which assessments are pending (Table 1).

MDH added eighteen pesticides of interest after reviewing the list.

Nine of the pesticides have high sales data (more than 100,000 pounds sold in Minnesota/year). These high-volume

sales pesticides are clethodim, fluazifop, glyphosate, mancozeb, MCPP-p, nitropyrin, permethrin, piperonyl butoxide, and thiophanate methyl.

Fipronil was of interest to MDH because of past collaboration with MDA related to an indoor misuse case, and flufenacet (parent) was added because MDA included flufenacet OXA (degradate) on the list.

MDH added seven pesticide degradates because a parent pesticide was on the MDA list and information from the review of the parent indicated that the degradate might be more toxic than the parent. The additional degradates were disulfoton sulfoxide, ETU (ethylenethiourea), malaoxon, omethoate, phorate sulfone, phorate sulfoxide, and TPA (tetrachloroterephthalic acid).

Sources of data

Sufficient USEPA or Cal EPA data were available to complete rapid assessments for all but four of the chemicals listed in Appendix A. USEPA HHBPs were available for 37 percent of the 159 chemicals evaluated. Acute and chronic HHBPs for the chemicals on the list were compared and MDH confirmed that chronic RfDs developed by USEPA for HHBPs were at least as protective as USEPA acute RfDs. Therefore, PODs based on chronic data were used to derive the rapid assessment results. Additional literature searches for at least six chemicals produced information that MDH used to select uncertainty factors.

Number of rapid assessments completed

Fourteen chemicals did not have sufficient data to complete a chemical specific rapid assessment, but MDH determined that MDA should use the result of the rapid assessment of another chemical (e.g., the parent pesticide of an environmental degradate) for risk assessments (Table 2). For the purposes of this report, the 14 chemicals for which MDH recommends a surrogate are included in the totals for the rapid assessments completed.

Of the 159 chemicals evaluated, four chemicals (Total Petroleum Hydrocarbons, Ammonia, Dibenzofuran, and Neburon) did not have appropriate or sufficient data to conduct a rapid assessment. In total, 155 chemicals (including the chemicals for which MDH recommends a surrogate for cancer or non-cancer endpoints) had sufficient data to complete a rapid assessment for non-cancer, cancer, or both health endpoints.

Results of the rapid assessments

Implementing current MDH risk assessment methodology resulted in differences between the rapid assessment result and USEPA HHBP values and differences between many existing, but outdated, MDH guidance values.

a) Cancer

Assessments for cancer were completed for 34 chemicals (22 percent of 155 assessments). Four of the 34 chemicals (Alpha-BHC, Beta BHC, Carbazole, and Diallate) did not have enough data to also derive a non-cancer assessment. Of the 30 chemicals that were assessed for both cancer and non-cancer endpoints, the cancer endpoint yielded the lower (more conservative) result for 15 chemicals and the non-cancer endpoint yielded the lower result for 15 chemicals. Cancer would be, therefore, the likely basis of risk assessment guidance for 19 of the 155 chemicals assessed.

The 34 chemicals with cancer rapid assessments were fairly equally represented by insecticides (41%), herbicides

(32%), and fungicides (21%). The other six percent of the chemicals were agricultural-related, non-pesticides such as Polycyclic Aromatic Hydrocarbons (PAHs).

b) Non-cancer

Assessments for non-cancer endpoints were completed for 151 chemicals (97 percent of 155 assessments). As mentioned above, there were four chemicals for which only cancer data were available.

One to five health endpoints may have been identified for each chemical. The most sensitive endpoints and the basis of 59 percent of the assessments were effects on the liver and nervous system. Other health endpoints included effects on kidneys, blood, thyroid and development. The most commonly affected organ system in studies of insecticides was the nervous system. For herbicides, the health endpoints were more varied and included the liver and kidneys (among others). Fungicides affected, most commonly, the thyroid and liver. Health endpoints associated with the non-pesticide agricultural chemicals included the liver, kidney, and nervous system.

There were five reasons that an Uncertainty Factor (UF) (including the dose adjustment factor related to interspecies extrapolation) was used in the non-cancer rapid assessments.

- A UF for intraspecies variation was used in all assessments.
- A UF for interspecies uncertainty and a DAF was used for all assessments based on animal studies. Only one POD (for the pesticide Propoxur) was based on a human study and no DAF or UF was required.
- A UF was used in five percent of assessments to account for the use of a LOAEL rather than a NOAEL.
- A UF was used in 35 percent of the assessments to account for sub-chronic to chronic extrapolation in toxicity test results. A common example of this was for assessments where the critical study was a 1-year dog toxicity study instead of a two-year dog study or chronic rodent study.
- UFs were often added to assessments because of deficiencies in the toxicity database (26 percent). USEPA often cited lack of a reproductive or developmental study as a reason to use a database UF.

A total UF of 300 (or less) was used in 94 percent of the non-cancer assessments, which is an indication that there was a basic set of toxicity data for most pesticides.

Surrogate approach

There were seven environmental degradates with sufficient toxicity data to derive a rapid assessment. These include: aldicarb sulfone, aldicarb sulfoxide, ETU, hydroxyatrazine, dimethoate oxon, malaoxon, and phorate sulfoxide.

The rapid assessments (non-cancer and cancer) of surrogate chemicals (a structurally similar chemical such as the parent of an environmental degradate) are recommended for 14 chemicals: DDD, DDE, diazinon oxon, disulfoton sulfone, disulfoton sulfoxide, flufenacet OXA, imazamethabenz acid, isoxaflutole DKN, methyl paraoxon, norflurazon – desmethyl, phorate sulfone, propachlor ESA, propachlor OXA, and TPA. Additionally, data for a surrogate chemical (degradate ETU) was used to derive the cancer rapid assessment for maneb and mancozeb.

MDH found information indicating that the environmental degradates of some pesticides were potentially more toxic than the parent pesticide. These degradates include: Diazinon Oxon, Disulfoton Sulfone, Disulfoton Sulfoxide, Methyl Paraoxon, and Phorate Sulfone. For each of these five degradates, MDH recommends the rapid assessment of the parent pesticides. However, at this time MDH is working on a proposed method for conducting rapid assessments for degradates that may be more toxic than the parent pesticides. When this evaluation is completed,

MDH will provide MDA with quantitatively adjusted rapid assessment results. Based on a preliminary view of the data, the rapid assessments for at least some degradates will likely be lower than the result for the parent.

Discussion

Rapid assessment results are appropriately conservative

Rapid assessment methods were designed to provide a conservative (protective) evaluation of potential risk. Rapid assessments were developed using assumptions that were potentially more protective than the nuanced and careful selection of doses and exposures that are made in the course of a full, in-depth chemical review that is carried out to develop Health Risk Limits (HRLs), Risk Assessment Advice (RAA), and Health-Based Values (HBVs). MDH assumed rapid assessments (particularly non-cancer assessments) were likely to be lower in value than a corresponding HRL, RAA, or HBV. Of the 155 chemicals with rapid assessments (non-cancer or cancer), 140 chemicals had other MDH guidance and/or recent USEPA guidance values (such as the HHBPs). A comparison of results of the rapid assessments and other guidance values indicates that rapid assessments were equal or lower in value than existing MDH or USEPA assessment for 121 of 140 chemicals (86 percent). For example, for the 59 pesticides that had non-cancer HHBPs, the results of rapid assessments were lower than the corresponding HHBPs by a factor ranging from 1.1 to more than 100. The results of the rapid assessments were lower than 91 percent of the corresponding existing but outdated MDH guidance.

There are several reasons why the non-cancer rapid assessments provide more conservative results than previous guidance values (including HHBPs). One reason for this is the intake rate of 0.289 L/kg-d in current practice that was not in use prior to 2008, when the intake rate of 2L/70 kg or 28.6 L/kg-d was typically used. However, the high infant intake rate is used with a relative source contribution factor of 0.5 rather than the default of 0.2 used in the past. As a result the net change just due to a change in exposure is a factor of 4 (that is, a four-fold lower drinking water value compared to the algorithms used prior to 2008). Another reason for a more conservative outcome than in the past is that MDH currently uses a wider range of database uncertainties and may be using a sub-chronic to chronic uncertainty factor when the point of departure is based on a one-year dog study. The use of DAFs rather than a full 10-fold uncertainty factor for use of an animal study may also account for differences in past MDH assessments and current HHBPs. Of the three cases in which MDH chose a different POD than was used by USEPA to calculate an HHBP, the largest difference was in the case of bromoxynil, where a 5-fold lower POD was used to derive the rapid assessment than was used in the HHBP.

In 12 cases the results of the rapid assessments were higher than existing MDH values by a factor of up to 3.5 fold. There are several reason for this, but most often the difference was due to the historic use of a 10-fold uncertainty factor when the chemical was classified as possible carcinogen but could not be assessed using a cancer slope factor. The other major reason for the higher rapid assessment result was that newer USEPA assessments and new toxicity data indicated that the chemical was less toxic than previously thought.

A major difference in the MDH rapid assessment for carcinogens and the USEPA assessments was due to the difference in the incremental lifetime cancer risk. USEPA used an incremental risk ranging from one person in 10,000 to one in 1,000,000 to calculate the HHBPs for carcinogenic pesticides. In contrast, MDH used a mid-range incremental cancer risk of one in 100,000 to calculate the cancer assessments. Because of the wider range of cancer risk levels used by the USEPA, there were eight chemicals that had lower cancer HHBP values (based on the lower incremental risk level of one in 1,000,000) compared to the results from the MDH cancer rapid assessments. If USEPA

had used an increment risk of one in 100,000, none of the cancer HHBP values would have been lower than the cancer rapid assessment results. Another difference between USEPA and MDH cancer assessments was that MDH used the supplemental guidance for early life stage exposure to carcinogens, which tends to lower the resulting drinking water assessment by a factor of 3.

Uses for rapid assessments

Four potential uses for rapid assessments are described below.

1) Setting priorities for full chemical reviews and environmental monitoring:

Rapid assessments may be compared with measured (or modeled) pesticide levels in groundwater and surface water to provide drinking water hazard quotients (the ratio of the measured chemical concentration in groundwater divided by the rapid assessment result) that are useful in conducting screening level assessments. The hazard quotients can be used to determine the need for additional monitoring of groundwater and surface water sources, and the need for in-depth MDH chemical reviews.

2) Setting remediation goals:

Rapid assessments provide a screening level risk characterization that can be used to evaluate the need for further site investigation and remediation or other health protections. Concentrations of groundwater contaminants that are at or below the rapid assessment results suggest that no further action is required.

At locations where multiple chemicals have been detected, the hazard quotient for each measured chemical, should be calculated and the hazard quotients added (the result is called a hazard index). A cumulative ratio greater than 1 suggests cumulative assessments by individual health endpoints should be evaluated. If there are health endpoints in common among the chemicals, such as cancer, nervous system, liver, kidneys, or endocrine system, endpoint-specific hazard indices can be calculated. Assessing cumulative risk by common health endpoints is a widely used and acceptable practice that often yields a lower cumulative risk from a mixture than adding all the quotients regardless of endpoint. MDH should be consulted concerning identifying health endpoints for evaluating cumulative exposures.

3) Developing health advice:

In situations where MDA wishes to use the results from rapid assessments to evaluate risk to human health, MDH requests the opportunity to consult with MDA, especially in cases where multiple chemicals are involved and cumulative assessments may be warranted. At locations where an individual or multiple chemicals have been detected and the hazard quotient is greater than 1, MDH should be consulted to aid in the interpretation of the results and assist in making recommendations to the public.

4) Developing analytical detection limits:

Rapid assessments may be useful in determining adequate detection and/or quantification limits for groundwater and surface water monitoring in Minnesota.

Rapid assessments over time

MDH has established expiration dates for the different types of health-based guidance, typically five years from the time the value was developed. Upon expiration, MDH conducts a literature and methodological review to determine if new information would alter the assessment.

MDH recommends a three to five-year expiration date for the rapid assessments, at the discretion of MDA and in accordance to MDA knowledge of changes to the toxicity database for any chemical of interest. Similarly, MDH intends to inform MDA of any changes in MDH methods and practice that would warrant a review or recalculation of rapid assessments.

Data sources that would prompt new reviews or reevaluations might include USEPA release of new HHBPs, new REDs or other regulatory actions, or other significant findings for individual pesticides or classes of pesticides.

MDH found toxicity data lacking for environmental degradates and recommends MDA contact MDH when new data on degradates come to the attention of MDA.

MDH identified four chemicals for which so little information was available that a rapid assessment could not be conducted. MDH identified another 14 chemicals for which adequate data were only available for a surrogate chemical (a structurally similar chemical such as the parent of an environmental degradate). New, alternative methods developed within the Contaminants of Emerging Concern program will soon be available to test possible alternative guidance development methods for these two sets of chemicals.

Summary and recommendations

Rapid assessments provide an efficient, transparent, and protective method for evaluating health risks associated with exposure to pesticides and other chemicals found in drinking water. However, compared to guidance values from full MDH chemical reviews, there is more uncertainty and conservatism in the results of rapid assessments.

Four major uses for rapid assessments include:
1) prioritizing chemicals for full MDH chemical reviews and environmental monitoring,
2) developing remediation goals,
3) providing advice to the public, and
4) developing analytical detection limits.

MDH should be consulted on the use of rapid assessments and interpretation of the results, especially for mixtures of chemicals where cumulative assessments may be warranted.

Because new toxicity data and in-depth health assessments are continually generated through USEPA and others, MDH recommends that rapid assessments be updated periodically (e.g., evaluated every five years for chemicals that are monitored or found in site investigations).

MDH appreciates MDA's interest in having access to current and high quality guidance that can be used to protect potential sources of drinking water. MDH intends to use the results of rapid assessments to consult with MDA on contaminant review prioritization and high-quality guidance for the highest priority chemicals on the MDA list.

Table 1: Pesticides listed by MDA for which current assessments were available[1] or are pending[2]

Pesticide	Current Guidance
Acetochlor	HRL 2009
Alachlor	HRL 2009
Alachlor ESA	RAA 2009
Alachlor OXA	RAA 2009
Atrazine	Review pending EPA assessment, 2009 HRL available
DEDI Atrazine	Pending (assess as triazine class)
Disopropylatrazine	Pending (assess as triazine class)
Desethylatrazine	Pending (assess as triazine class)
Chlorpyrifos	HBV 2013
Chlorpyrifos oxon	RAA 2013
Cyanazine	HRL 2009
Cyanazine acid	Use parent
Cyanazine amine	Use parent
Deethylcyanazine acid	Use parent
Simazine	Pending (assess as triazine class)
1,3,5-Trimethylbenzene	HRL 2009
Propazine	Pending (assess as triazine class)

[1] http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html
[2] http://www.health.state.mn.us/divs/eh/risk/review/index.html

Table 2: Pesticide degradates for which MDH recommends the non-cancer rapid assessment of a surrogate chemical

Degradate/Metabolite	Surrogate
DDD (p,p'-Dichlorodiphenyldichloroethane) (CAS# 72-54-8)	DDT (p,p'-Dichlorodiphenyltrichloroethane) (CAS# 50-29-3)
DDE (p,p'-Dichlorodiphenyldichloroethylene) (CAS# 72-55-9)	DDT (p,p'-Dichlorodiphenyltrichloroethane) (CAS# 50-29-3)
Diazinon oxon (CAS# 962-58-3)	Diazinon (CAS# 333-41-5)
Disulfoton sulfone (CAS# 249706-5)	Disulfoton (CAS# 298-04-4)
Disulfoton sulfoxide (CAS# 249707-6)	Disulfoton (CAS# 298-04-4)
Flufenacet OXA (CAS# 142459-58-3) (Parent)	Flufenacet (Thiaflumide) (CAS# 142459-58-3)
Imazamethabenz acid (CAS# 100728-84-5)	Imazamethabenz-methyl (CAS# 81405-85-8)
Isoxaflutole DKN (CAS# 141112-29-0) (Parent)	Isoxaflutole (CAS# 141112-29-0)
Methyl Paraoxon (CAS# 950-35-6)	Methyl Parathion (CAS# 298-00-0)
Norflurazon – desmethyl (CAS# 2376-24-1)	Norflurazon (CAS# 27314-13-2)
Phorate sulfone (CAS# 258804-7)	Phorate (CAS# 298-02-2)
Propachlor ESA (CAS# 947601-88-9)	Propachlor (CAS# 1918-16-7)
Propachlor OXA (no CAS#)	Propachlor (CAS# 1918-16-7)
TPA (Tetrachloroterephthalic Acid) (CAS# 2136-79-0)	DCPA (Dacthal) (CAS# 1861-32-1)

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Appendix A: Rapid Assessments Table

Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/ day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
2-4,D	94-75-7	70 (1993 HRL)	2	NA[5]	0.0014	Group D	Liver, kidney	CalEPA 2006c, CalEPA 2009b, USEPA 2005o
2,4-DB	94-82-6	60 (1995 HBV)	5	NA	0.0027	Not likely to be a human carcinogen	Body weight	USEPA 2005p
2,4,5-T	93-76-5	70 (1993 HRL)	10	NA	0.0081	Unknown	Developmental	USEPA 1989b
Acenaphthene	83-32-9	400 (1993 HRL)	40	NA	0.0245	Unknown	Liver, Kidney	MDH 2013, USDHHS 1995c, USEPA 1994a
Acetamiprid	135410-20-7	497 (HHBP)	100	NA	0.064	Not likely to be carcinogenic to humans	Liver, Body weight	USEPA 2012a
Aldicarb Sulfone	1646-88-4	1 (1993 HRL)	3	NA	0.00154	Unknown	ChE inhibition	USEPA 1993b, USEPA 1995a, USEPA 2007n
Aldicarb Sulfoxide	1646-87-3	1 (1993 HRL)	2	NA	0.000958	Unknown	ChE inhibition	USEPA 1995a, USEPA 2007n, Weil and Carpenter 1968
Aldrin	309-00-2	0.02 (1997 HBV)	0.04	0.006	0.0000225	Group B2	Liver	USEPA 1993c, USEPA 2003b
Alpha -BHC	319-84-6	0.06 (1997 HBV)	NA	0.02	NA	Group B2	NA	USEPA 1993d
Ammonia	7664-41-7	30,000 (HA)	Insufficient data	NA	NA	Unknown	Unknown	USEPA 2012n
Anthracene	120-12-7	2,000 (1993 HRL)	200	NA	0.14	Group D	Unknown	USEPA 1993e, USEPA 2012b

[1] HRL = Health Risk Limits, HBV = Health-Based Values, RAA = Risk Assessment Advice, HA = Health Advisory, HHBP = Health Benchmark for Pesticides, MCL = Maximum Contaminant Level, DWLOC = Drinking Water Levels of Comparison.

[2] USEPA Cancer Categories: Group A: Human carcinogen, Group B1: Probable human carcinogen – based on limited evidence of carcinogenicity in humans, Group B2: Probable human carcinogen – based on sufficient evidence of carcinogenicity in animals, Group C: Possible human carcinogen, Group D: Not classifiable as to human carcinogenicity, Group E: Evidence of non-carcinogenicity for humans

[3] MDH should be consulted before Health Effects are used in additive risk assessments.

[4] References provided upon request.

[5] Not Available.

Appendix A: Rapid Assessments Table

Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Azoxystrobin	131860-33-8	1,260 (HHBP)	300	NA	0.162	Not Likely to be carcinogenic to humans	Body weight, Bile duct	USEPA 2012c
Benfluralin	1861-40-1	35 (HHBP)	8	NA	0.0045	Suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential	Kidney	USEPA 2003a
Bensulfuran – methyl	83055-99-6	1,400 (HHBP)	50	NA	0.028	Unknown	Liver	USEPA 1997a
Bentazon	25057-89-0	200 (1998 HBV)	8	NA	0.0045	Group E	Gastrointestinal, Blood	USEPA 1994d, USEPA 1998a
Beta-BHC	319-85-7	0.2 (1997 HBV)	NA	0.06	NA	Group C	NA	USEPA 1993f
Bifenthrin	82657-04-03	NA	3	2	0.00182	Group C	Nervous system	CalEPA 1997, USEPA 2011a
Boscalid	188425-85-6	1,526 (HHBP)	300	NA	0.196	Suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential	Liver, Thyroid	USEPA 2010a
Bromacil	314-40-9	70 (HA)	30	NA	0.018	Group C	Body weight, Female reproductive system	USEPA 1992a, USEPA 1996d
Bromoxynil	1689-84-5	100 (1997 HBV) 105 (HHBP)	0.7	1	0.00042	Group C	Liver, Body weight	CalEPA 2005a, USEPA 1998e
Butylate	2008-41-5	300 (1996 HBV)	10	NA	0.007	Group E	Liver, Body weight	USEPA 1993a, USEPA 2001a

Appendix A: Rapid Assessments Table

Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Carbaryl	63-25-2	70 (2003 HBV)	10	100	0.00843	Likely to be carcinogenic in humans	ChE inhibition	CalEPA 2009a, USEPA 2007o, WDHS 2009
Carbazole	86-74-8	20 (2001 HBV)	NA	0.6	NA	Unknown	NA	CalEPA 2001, GWC 2011
Carbendazim (M BC)	10605-21-7	175 (HHBP) 15-1500 (Cancer HHBP)	9	40	0.00525	Group C	Liver	USEPA 2002a, USEPA 2002c
Carbofuran	1563-66-2	40 (MCL)	0.1	NA	0.000069	Not Likely to be carcinogenic to humans	ChE inhibition	USEPA 2006i, USEPA 2007p
Chloramben	133-90-4	100 (1994 HRL)	10	NA	0.0075	Unknown	Liver	USEPA 1988c
Chlorantraniliprole	500008-45-7	11,060 (HHBP)	1000	NA	0.79	Not likely to be Carcinogenic to Humans	Liver	USEPA 2008b, USEPA 2010b, USEPA 2010h
Chlorimuron-ethyl	90982-32-4	100 (1997 HBV)	20	NA	0.0126	Not Likely to be carcinogenic to humans	Blood	USEPA 1989a, USEPA 2004h, USEPA 2009a, USEPA 2009b
Chlorothalonil	1897-45-6	30 (1993 HRL)	50	6	0.0315	Likely to be carcinogenic in humans	Kidney	CalEPA 2012, USEPA 1988d
Chlorpropham	101-21-3	400 (2002 HBV)	200	NA	0.105	Group E	Thyroid	USEPA 1996e, USEPA 2002f
Chlorsulfuron	64902-72-3	300 (1997 HBV)	20	NA	0.0135	Group E	Body weight	USEPA 2002b, USEPA 2005n
Chromium III	16065-83-1	20,000 (1994 HRL)	2,000	NA	1.32	Group D	Unknown	CalEPA 2011, USDHHS 2012a, USDHHS 2012c, USEPA 1998b, USEPA 2000a

Appendix A: Rapid Assessments Table

Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Chromium VI	18540-29-9	100 (1993 HRL)	0.7	0.2	0.00042	Group A (inhalation route) Group D (oral route)	Gastrointestinal	Cal EPA 2011, USDHHS 2012a, USDHHS 2012c, USEPA 1998c, USEPA 2000a
Clethodim	99129-21-2	70 (HHBP)	2	NA	0.0014	Not likely to be carcinogenic to humans	Liver, Blood	USEPA 2010c, USEPA 2010i
Clomazone (Dimethazone)	81777-89-1	300 (1997 HBV)	70	NA	0.0387	Not likely to be carcinogenic to humans	Liver	Cal EPA 2002, USEPA 1999b
Clopyralid	1702-17-6	1,050 (HHBP)	200	NA	0.135	Not likely to be carcinogenic to humans	Gastrointestinal	USEPA 2009c
Clothianidin	210880-92-5	686 (HHBP)	200	NA	0.0882	Not likely to be carcinogenic in humans	Developmental	USEPA 2012e
Cumene (Iso-propybenzene)	98-82-8	300 (1993 HRL)	40	NA	0.0253	Group D	Kidney	IPCS 1999, USDHHS 2012b, USEPA 1997f, USEPA 1997j
Cyfluthrin	68359-37-5	168 (HHBP)	6	NA	0.00336	Not likely to be a carcinogenic to humans	Nervous system	USEPA 2007c
Dacthal (DCPA)	1861-32-1	70 (2000 HBV)	20	70	0.009	Group C	Respiratory system, Liver, Thyroid	USEPA 1998f, USEPA 2008d, USEPA 2008h
DDD (p,p'-Di-chlorodiphenyl-dichloroethane)	72-54-8	See DDT	See DDT	0.4	See DDT	Group B2	See DDT	USDHHS 2002, USEPA 1988f

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Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
DDE (p,p'-Dichlorodiphenyldichloroethylene)	72-55-9	See DDT	See DDT	See DDT	See DDT	See DDT	See DDT	USDHHS 2002, USEPA 1988g
DDT (p,p'-Dichlorodiphenyltrichloroethane)	50-29-3	1 (1993 HRL)	0.07	0.3	0.0000383	Group B2	Liver	USDHHS 2002, USEPA 1996c
Diallate	2303-16-4	6 (1995 HBV)	NA	2	NA	Group C	NA	HSDB 2003, Lorenzo, Staniano & Silengo 1978, USEPA 1986, USEPA 1983, USEPA 1984, USEPA 1997d
Diazinon	333-41-5	1 (HA)	0.08	NA	0.000048	Group E	ChE inhibition	Sparling & Fellers 2007, USDHHS 2008b, USDHHS 2009a, USDHHS 2009b, USEPA 1988a, USEPA 1999a, USEPA 2006g, USEPA 2006p
Diazinon oxon	962-58-3	See Diazinon	See Diazinon	See Diazinon	See Diazinon	See Diazinon	See Diazinon	See Diazinon
Dibenzofuran	132-64-9	20 (2001 HBV)	Insufficient data	NA	NA	Group D	Unknown	USDHHS 2000,USEPA 1988e
Dicamba	1918-00-9	200 (1993 HRL)	700	NA	0.405	Not likely to be carcinogenic to humans	Developmental	USEPA 1995g, USEPA 2005a, USEPA 2006q, USEPA 2011c

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Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/ day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Dichlobenil (2,6-di-chlorobenzonitrile)	1194-65-6	70 (HHBP)	40	NA	0.021	Group C	Liver	USEPA 1998g, USEPA 2008c
Dichlorprop and Dichlorprop-p	120-36-5 and 15165-67-0	NA	60	NA	0.0324	Not likely to be carcinogenic to humans	Kidney	USEPA 2007q
Dichlorvos	62-73-7	4 (HHBP)	1	NA	0.0007	Suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential	ChE inhibition	USEPA 2006b
Dicrotophos	141-66-2	0.5 (HHBP)	0.03	NA	0.000018	Suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential	ChE inhibition	USEPA 2001b, USEPA 2006r, USEPA 2001c
Dieldrin	60-51-1	0.006 (2009 HRL)	0.08	0.006	0.000045	Group B2	Liver	USEPA 2003b
Difenoconazole	119446-68-3	70 (HHBP)	10	NA	0.00864	Group C	Developmental	PPDB 2011, USEPA 2010d
Dimethoate	60-51-5	1 (1996 HBV) 15 (HHBP)	3	NA	0.00198	Group C	ChE inhibition	USEPA 1990a, USEPA 2006c, USEPA 2006h
Dinotefuran	165252-70-0	140 (HHBP)	5	NA	0.0028	Not likely to be carcinogenic to humans	Thymus	(USEPA 2009) (USEPA 2013)

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Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Disulfoton	298-04-4	0.3 (1994 HRL)	0.3	NA	0.000182	Group E	ChE inhibition	HSDB 2006, IPCS 1973, USDHHS 1995a, USEPA 2006s, USEPA 2008a
Disulfoton sulfone	249706-5	See Disulfoton sulfone	See Disulfoton sulfone	See Disulfoton sulfone	See Disulfoton sulfone	See Disulfoton sulfone	See Disulfoton sulfone	See Disulfoton sulfone
Disulfoton sulfoxide	249707-6	0.3 (1994 HRL)	0.3 /3	NA	0.000182	Group E	ChE inhibition	HSDB 2006, IPCS 1973, USDHHS 1995a, USEPA 2006s, USEPA 2008a
Diuron	330-54-1	5 (2008 RAA)	2	5	0.0009	Likely to be carcinogenic to humans	Blood	USEPA 2003, Bauer et al. 1989, Chen and Young 2009, USEPA 2007, USEPA 2010
Endosulfan	115-29-7	40 (1999 HBV)	0.9	NA	0.00054	Not likely to be carcinogenic to humans	Kidney, Body weight	IARC 2012, USDHHS 2011, Silva and Beauvais 2010, USDHHS 2013, USEPA 1994b, USEPA 2002g
EPTC (S-Ethyl dipropylthio-carbamate)	759-94-4	200 (HRL 1993)	80	NA	0.045	Not likely to be carcinogenic to humans	Nervous system, Body weight	CalEPA 1995, USEPA 1999f, USEPA 1999h, USEPA 2011b, USGS 2010
Esfenvalerate	66230-04-4	13 (HHBP)	2	NA	0.0013	Group E	Nervous system	USEPA 2004a

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Ethafluralin	55283-68-6	300 (HBV 1999), 280 (HHBP), 0.4 - 40 (Cancer HHBP)	10	1	0.0056	Group C	Blood, Liver	USEPA 2007d
Ethofumesate	26225-79-6	1,980 (HHBP)	800	NA	0.45	Not likely to be carcinogenic to humans	Developmental	USEPA 2006d, FAO 2007
ETU (Ethylenethio-urea)	96-46-7	NA	0.1	2	0.0000756	Group B2	Thyroid	HSDB 2010, USEPA 1991a, USEPA 1996b, USEPA 2013b
Fipronil	120068-37-3	1 (HHBP)	0.3	NA	0.00017	Group C	Nervous system, Thyroid	USEPA 1994h, USEPA 2007a
Fluazifop	69806-50-4	52 (HHBP)	10	NA	0.0057	Not likely to be carcinogenic to humans	Male and female reproductive system, Blood	USEPA 2004b, USEPA 2004d
Flufenacet	142459-58-3	12 (HHBP)	2	NA	0.0013	Not Likely to be carcinogenic to humans	Developmental, Body weight	USEPA 2007e, USEPA 2007f
Flufenacet OXA	See Flufenacet	See Flufenacet	See Flufenacet	See Flufenacet	See Flufenacet	See Flufenacet	See Flufenacet	See Flufenacet
Flumetsulam	98967-40-9	7,000 (HHBP)	400	NA	0.21	Group E	Kidney, Liver	USEPA 2004c
Fluoranthene	206-44-0	300 (1993 HRL)	10	NA	0.0058	Group D	Liver	CalEPA 2004b, USDHHS 1995b, USEPA 1994c
Fluorene (9H-Fluorene)	86-73-7	300 (1993 HRL)	10	NA	0.0058	Group D	Blood	USDHHS 1995b, USEPA 1994c
Flutriafol	76674-21-0	350 (HHBP)	10	NA	0.007	Not likely to be carcinogenic to humans	Liver, Blood, Body weight, Adrenal	USEPA 2012j, USEPA 2012k

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Fonofos	944-22-9	10 (1995 HBV)	0.5	NA	0.00028	Group E	ChE inhibition, blood, Liver, Gastrointestinal	USEPA 1999g, USEPA 2008e
Glyphosate	1071-83-6	NA	1000	NA	0.7875	Group E	Survival, Endocrine system, Gastrointestinal	USEPA 1993i
Halosulfuron – methyl	100784-20-1	700 (HHBP)	20	NA	0.014	Not likely to be carcinogenic to humans	Body weights	USEPA 2010g, USEPA 2010j
Hexazinone	51235-04-2	200 (1995 HBV)	10	NA	0.007	Group D	Liver	USEPA 1994e
Hydroxyatrizine	2163-68-0	20 (2005 HBV)	20	NA	0.009	Unknown	Kidney	USEPA 1996a, USEPA 2007b
Imazamethabenz acid (Degra-date of Imaza-methabenz-methyl)	100728-84-5	NA	See Imaza-methabenz-methyl	See Imaza-methabenz-methyl	See Imaza-methabenz-methyl	See Imaza-methabenz-methyl	See Imaza-methabenz-methyl	See Imaza-methabenz-methyl
Imazamethabenz-methyl	81405-85-8	1,750 (HHBP)	60	NA	0.035	Group D	Body weights	USEPA 2005d, USEPA 2004e, USEPA 2005m
Imazamox	114311-32-9	104,980 (DWLOC)	20,000	NA	13.2	Not likely to be carcinogenic to humans	Unknown	USEPA 2001e
Imazapic	104098-48-8	3,500 (HHBP)	30	NA	0.01918	Group E	Muscle (skeletal)	USEPA 2001f

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Imazapyr	81334-34-1	17,500 (HHBP)	900	NA	0.525	Group E	NA	USEPA 2005e, USEPA 2005f, USEPA 2006e, USEPA 2006t, USEPA 2008f
Imazaquin	81335-37-7	1,750 (HHBP)	60	NA	0.035	Not likely to be carcinogenic to humans	Muscle (skeletal), Blood, Bodyweight	USEPA 2005g, USEPA 2005b
Imazethapyr	81335-77-5	17,500 (HHBP)	900	NA	0.525	Not likely to be carcinogenic to humans	NA	USEPA 2005e, USEPA 2005f, USEPA 2006e, USEPA 2006t, USEPA 2008f
Imidacloprid	138261-41-3	399 (HHBP)	90	NA	0.0513	Group E	Thyroid	Bal et al. 2012, CalEPA 2006a, CalEPA 2006b, Gawade et al. 2013, USEPA 1997e, USEPA 2010f, USEPA 2010k
Isoxaflutole	141112-29-0	140 (HHBP) 3-300 (Cancer HHBP) 10 (2003 HBV)	7	9	0.004	Likely to be carcinogenic to humans	Liver, Eyes, Nervous system, Developmental	USEPA 1997g, USEPA 2006l, USEPA 2011d
Isoxaflutole DKN	See Isoxaflutole	See Isoxaflutole	See Isoxaflutole	See Isoxaflutole	See Isoxaflutole	See Isoxaflutole	See Isoxaflutole	USEPA 1989c, USEPA 1997g, USEPA 2006l, USEPA 2011d
Lambda Cyhalothrin	91465-08-6	7 (HHBP)	0.2	NA	0.00014	Not likely to be carcinogenic to humans	Nervous system	USEPA 2007g, USEPA 2007j

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Chemical	CAS# (Chemical Abstrasts Service)	MDH Guidance Value and/ or Other (ug/L)[1]	Rapid Assessment Non-Cancer (ug/L)	Rapid Assessment Cancer (ug/L)	RfD (mg/kg/day)	Cancer Classification (USEPA)[2]	Non-Cancer Health Effects (Critical Effects)[3]	References[4]
Linuron	330-55-2	1 (1993 HRL)	2	NA	0.0011	Group C	Blood	CalEPA 2013, USEPA 1995e
Malaoxon	1634-78-2	100 (1996 HBV)	2	NA	0.0009	Unknown	ChE inhibition	Sparling & Fellers 2007, USEPA 2006u
Malathion	121-75-5	100 (1996 HBV)	100	NA	0.0544	Suggestive evidence of carcinogenic potential	ChE inhibition	Choudhary, Goyal & Joshi 2008, Sparling & Fellers 2007, USDHHS 2003, USEPA 1999d, USEPA 2006u
Mancozeb	801801-7	35 (HHBP) 0.6 - 60 (Cancer HHBP)	8	See ETU	0.00437	See ETU	Thyroid	USEPA 2007k, USEPA 2013c, USEPA 2007h, Xu 2000
Maneb	12427-38-2	350 (HHBP) 0.6 - 60 (Cancer HHBP)	70	See ETU	0.038	See ETU	Thyroid	USEPA 2005i
MCPA (2-methyl-4-chlorophenoxyacetic acid)	94-74-6	3 (1993 HRL)	7	NA	0.00396	Not likely to be carcinogenic to humans	Liver, Kidney	Health Canada 2009, USEPA 2004f, USEPA 2004k
MCPB [4-(2-Methyl-4-chlorophenoxy) butyric acid]	94-81-5	70 (1997 HBV)	7	NA	0.0039	Not likely to be carcinogenic to humans	Liver, Kidney	USEPA 2006m

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MCPP (Mecprop) (methylchloro-phenoxy-propi-onic acid)	93-65-2	7 (1996 HBV)	4	NA	0.0023	Unknown	Kidney	USEPA 1990b, USEPA 2007r
MCPP-p	16484-77-8	NA	30	NA	0.02	Unknown	Liver, Kidney	USEPA 1990b, USEPA 2007r
Mesotrione	104206-82-8	49 (HHBP)	5	NA	0.00315	Not likely to be carcinogenic to humans	Developmental, Eyes	USEPA 1995b, USEPA 2009g
Metalaxyl	57837-19-1	NA	20	NA	0.0088	Group E	Liver	USEPA 1994g, USEPA 1995c
Methamidophos	10265-92-6	0.3 (1999 HBV)	0.04	NA	0.000023	Not likely to be carcinogenic to humans	ChE inhibition	CalEPA 2005b, USEPA 2006v
Methoxychlor	72-43-5	40 (MCL)	10	NA	0.0075	Group D	Developmental	CalEPA 2010, USEPA 1991b, USEPA 2004g
Methyl paraoxon	950-35-6	See Methyl parathion	See Methyl parathion	See Methyl parathion	See Methyl parathion	See Methyl parathion	See Methyl parathion	See Methyl parathion
Methyl parathion	298-00-0	2 (1996 HBV)	0.08	NA	0.000046	Not likely to be carcinogenic to humans	Blood, ChE inhibition	CalEPA 1999, CalEPA 2004a, USEPA 1991c, USEPA 2006j, USEPA 2006w
2-Methylphenol (o-cresol)	95-48-7	30 (1993 HRL)	70	NA	0.038	Group C	Body weight, Nervous system	USDHHS 2008a, USEPA 1992b, USEPA 2006a
3-Methylphenol (m-cresol)	108-39-4	30 (1993 HRL)	70	NA	0.038	Group C	Body weight, Nervous system	USDHHS 2008a, USEPA 1992c, USEPA 2006a

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4-Methylphenol (p-cresol)	106-44-5	3 (1994 HRL)	10	NA	0.0075	Group C	Nervous system, Respiratory system	TYL 1988, USDHHS 2008a, USEPA 1994f, USEPA 1997b, USEPA 1997c, USEPA 2006a
Metsulfu-ron-methyl	74223-64-6	2,000 (1997 HBV)	400	NA	0.225	Unknown	Body weight	USEPA 1988b
Myclobutanil	88671-89-0	175 (HHBP)	40	NA	0.0224	Group E	Male reproductive system	USEPA 2007l, USEPA 2007i
Neburon	555-37-3	NA	Insufficient data	NA	NA	Unknown	Unknown	NA
Nicosulfuron	11191-09-4	9000 (1997 HBV)	300	NA	0.175	Not likely to be carcinogenic to humans	Liver, Kidney, Body weight	USEPA 2004i, USEPA 2010e, USEPA 2011e, USEPA 2012m
Nitrapyrin	1929-82-4	210 (HHBP)	7	NA	0.0042	Suggestive evidence of carcinogenic potential	Liver	USEPA 2005r, USEPA 2012l
Norflurazon	27314-13-2	105 (HHBP)	4	NA	0.0021	Group C	Liver	USEPA 1996f, USEPA 2001d, USEPA 2001g
Norflurazon – desmethyl	2376-24-1	See Norflurazon	See Norflurazon	See Norflurazon	See Norflurazon	See Norflurazon	See Norflurazon	USEPA 1996f, USEPA 2001d, USEPA 2001g
Omethoate (Dimethoate Oxon)	1113-02-6	NA	0.6	NA	0.00036	Group C	ChE inhibition	USEPA 1990a, USEPA 2006c, USEPA 2006h

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Oxadiazon	19666-30-9	NA	6	1	0.00324	Likely to be carcinogenic to humans	Liver	USEPA 2003c
Oxydematon - methyl (ODM)	301-12-2	0.7 (HHBP)	0.3	NA	0.000175	Group E	ChE inhibition	USEPA 1999c, USEPA 1999e, USEPA 2005h, USEPA 2006x
Pendimethalin	40487-42-1	210 (HHBP), 90 (HBV1995)	40	NA	0.023	Group C	Thyroid	USEPA 2009k
Pentachloroni-trobenzene	82-68-8	20 (1997 HBV)	1	NA	0.00077	Group C	Liver, Thyroid	USEPA 2006y
Permethrin	52645-53-1	1,750 (HHBP) 4 - 400 (Cancer HHBP)	30	10	0.019	Likely to be carcinogenic to humans	Nervous system	USEPA 2009h, Vadhana et al. 2013
Phorate	298-02-2	1 (1995 HBV)	1	NA	0.0007	Group E	ChE inhibition	HSDB 2005, IPCS 1977b, USEPA Appendix 1HED Effects, USEPA 2006z, USEPA 2006k, USEPA 2013a
Phorate sulfone	258804-7	NA	See Phorate	See Phorate	See Phorate	See Phorate	See Phorate	See Phorate
Phorate sulfoxide	258805-8	NA	0.02	NA	0.0000123	Group E	ChE inhibition	Hoffman et al. 2002, IPCS 1977b, USEPA 2006k, HSDB 2005
Phostebupirim (Tebupirim-phos)	96182-53-5	0.1 (HHBP)	0.07	NA	0.000042	Not likely to be carcinogenic to humans.	ChE inhibition	USEPA 2000b, USEPA 2000c, USEPA 2006f, USEPA 2009m

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Picloram	1918-02-1	500 (HRL 1993)	300	NA	0.18	Group E	Liver	USEPA 1995d, USEPA 1995f
Piperonyl Butoxide	51-03-6	1,085 (HHBP)	40	NA	0.0217	Group C	Liver	USEPA 2005c, USEPA 2005j
Primisulfuron-methyl	86209-51-0	20 (1997 HBV)	60	NA	0.035	Group D	Blood, Liver, Thyroid	USEPA 2002e
Prometon	1610-18-0	100 (HRL 1993)	10	NA	0.007	Not likely to be carcinogenic to humans	Body weight	USEPA 2008i
Prometryn	7287-19-6	280 (HHBP)	100	NA	0.0788	Group E	Liver, Kidney, Skeletal	USEPA 2009j, USEPA 2009e
Propachlor	1918-16-7	90 (1993 HRL)	15	3	0.0086	Likely human carcinogen (or B2)	Body weight	USEPA 1998h
Propachlor ESA	947601-88-9	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor
Propachlor OXA	NA	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor	See Propachlor
Propiconazole	60207-90-1	700 (HHBP) 90 (2000 HBV)	90	NA	0.05	Group C	Liver	USEPA 2013e
Propoxur (Baygon)	114 -26-1	NA	3	30	0.0015	Group B2	ChE inhibition	USEPA 1997h
Pydrin (Fenvalerate)	51630-58-1	200 (2000 HBV)	30	NA	0.019	Group E	Nervous system	USEPA 1992d
Pyrene	129-00-0	200 (1993 HRL)	20	NA	0.0105	Group D	Kidney	USEPA 1993g
Pyroxasulfone	447399-55-5	140 (HHBP)	5	NA	0.0028	Not likely to be carcinogenic to humans	Nervous system, Liver	USEPA 2012f
Saflufenacil	372137-35-4	322 (HHBP)	40	NA	0.023	Not likely carcinogenic to humans	Blood	BASF 2010, USEPA 2009i

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Siduron	1982-49-6	1,050 (HHBP)	200	NA	0.115	Unknown	Body weight	USEPA 2008j
Sulfometuron – methyl	74222-97-2	1,925 (HHBP)	100	NA	0.0578	Unknown	Body weight	USEPA 2008l
Tebuconazole	107534-96-3	203 (HHBP)	30	NA	0.02	Group C	Nervous system, Developmental	USEPA 2011f
Tembotrione	365400-11-9	3 (HHBP)	0.6	NA	0.00036	Suggestive evidence of carcinogenic potential	Eyes, Body weight, Kidney, Liver, Nervous system	CLH 2012, EFSA 2012, USEPA 2007m
Terbufos	13071-79-9	0.2 (HBV 1995)	0.1	NA	0.00007	Group E	Nervous system	USEPA 1999i, USEPA 2006aa, USEPA 2008g, USEPA 2012d
Tetraconazole	112281-77-3	51 (HHBP) 2- 200 Cancer (HHBP)	30	4	0.0153	Likely to be carcinogenic to humans	Kidney	USEPA 2011g
Thiamethoxam	153719-23-4	84 (HHBP)	20	NA	0.011	Not likely to be carcinogenic in humans	Developmental	European Comm. 2006, USEPA 2011h, USEPA 2012g
Thifensulfuron-methyl (Harmony)	79277-27-3	90 (1997 HBV)	70	NA	0.0387	Not likely to be a human carcinogen	Body weight	USEPA 2012h
Thiobencarb	28249-77-6	70 (HHBP)	20	NA	0.009	Group D	Body weight, Kidney	USEPA 1997i
Thiophanate Methyl	23564-05-8	187 (HHBP) 3-300 (Cancer HHBP)	6	9	0.00336	Likely to be carcinogenic to humans	Body weight, Thyroid	USEPA 2002a, USEPA 2002c, USEPA 2009f, USEPA 2009n

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TPA (Tetrachloroterephthalic Acid) (Degradate of Dacthal)	2136-79-0	NA	See Dacthal	See Dacthal	See Dacthal	See Dacthal	See Dacthal	See Dacthal
TPH (Total Petroleum Hydrocarbon)	NA	200 (1999 HBV)	NA	NA	NA	Unknown	Unknown	USDHHS 1999
Triallate	2303-17-5	9 (1995 HBV)	10	1	0.00675	Group C	Survival, Body weight, Adrenal	Lorenzo, Staniano & Silengo 1978, USEPA 2001h
Triasulfuron	82097-50-5	70 (1997 HBV)	10	NA	0.006	Group E	Liver	USEPA 1991d, USEPA 2012o
Tribenuron-methyl	101200-48-0	60 (1997 HBV)	0.6	NA	0.000336	Group C	Body weight, Liver	USEPA 2011i
Tributyltin oxide (TBTO)	56-35-9	2 (1999 HBV)	0.04	NA	0.000023	Group D	Immune system	USEPA 2008k
Triclopyr	55335-06-3	300 (1999 HBV)	80	NA	0.045	Group D	Kidney, Body weight	CalEPA 2000, USEPA 1998d, USEPA 1998i, USEPA 2002d, USEPA 2005s
Trifluralin	1582-09-8	5 (1995 HBV)	9	20	0.005	Group C	Body weight, Blood, Liver	Syracuse Environ. Research Association 2011, USEPA 1993h, USEPA 1996g, USEPA 2003d, USEPA 2004j
Zeta-Cypermethrin	97955-44-7	420 (HHBP)	50	NA	0.03	Group C	Nervous system	EFSA 2008, USEPA 2006o, USEPA 2012i
Zineb	12122-67-7	NA	40	NA	0.0225	Unknown	Thyroid	IPCS 1998, USEPA 1988h