MINNESOTA
MDH
DEPARTMENT OF HEALTH

Protecting, maintaining and improving the health of all Minnesotans

October 12, 2010

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St. Paul, Minnesota 55155

Re: In The Matter of the Proposed Rules of the State Department of Health Relating to the Health Risk Limits for Groundwater; *Minnesota Rules*, Chapter 4717, Parts 7860 and Part 7500; Governor's Tracking #AR 541

Dear Librarian:

The Minnesota Department of Health intends to adopt rules relating to the Health Risk Limits for Groundwater. We plan to publish a Dual Notice of Intent to Adopt Rules in the State Register on October 18, 2010.

The Department has prepared a Statement of Need and Reasonableness (SONAR) supporting the proposed rules. As required by *Minnesota Statutes*, sections 14.131 and 14.23, the Department is sending the Library an electronic copy of the Statement of Need and Reasonableness at the same time we are mailing our Dual Notice of Intent to Adopt Rules.

If you have questions, please contact me at (651) 201-4907.

Yours very truly,

Nitika Moibi
Planner Principal State
Division of Environmental Health
Minnesota Department of Health
P.O. Box: 64975
St. Paul, MN 55164

Enclosure: Statement of Need and Reasonableness

STATE OF MINNESOTA

Minnesota Department of Health

In the Matter of the Proposed Rules
Of the Minnesota Department of Health
Relating to Health Risk Limits for Groundwater,
Minnesota Rules, Chapter 4717, Part 7860 and Part 7500

STATEMENT OF NEED AND REASONABLENESS

October 2010

10/5/10
Date

Sanne Magnan, M.D., Ph. D.
Commissioner
Minnesota Department of Health
P.O. Box 64975
St. Paul, MN 55164

ABOUT THIS DOCUMENT

This Statement of Need and Reasonableness (SONAR) supports the Minnesota Department of Health's revision of its rules on the Health Risk Limits for Groundwater. The proposed rules are available at:

http://www.health.state.mn.us/divs/eh/risk/rules/water/rulerelated.html#draft

For questions or concerns regarding this document, please contact Nitika Moibi at nitika.moibi@state.mn.us or, call (651) 201-4907.

The proposed rules will be published in Minnesota's *State Register* at a later time. Subscribers of MDH's Groundwater Rules and Guidance subscription list will receive a notice of publication. For Minnesota's statutory procedure for promulgation of administrative rules, see *Minnesota Statutes*, section 14.001 et seq., and in particular, section 14.22.

Upon request, this SONAR can be made available in an alternative format, such as large print, Braille, or cassette tape. To make a request, contact Nitika Moibi at the Minnesota Department of Health, Division of Environmental Health, Section, 625 North Robert Street, PO Box 64975, St. Paul, MN 55164-0975, ph. (651) 201-4907, fax (651) 201-4606, e-mail: nitika.moibi@state.mn.us. TTY users may call the Minnesota Department of Health at (651) 201-5797.

MINNESOTA DEPARTMENT OF HEALTH

STATEMENT OF NEED AND REASONABLENESS
Proposed Amendments to the Rules on Health Risk Limits for Groundwater
(*Minnesota Rules*, Chapter 4717, Part 7860 and Part 7500)

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"It is the goal of the state that groundwater be maintained in its natural condition, free from any degradation caused by human activities."

Groundwater Protection Act, 1989, Chapter 103H

Introduction

The goal of the 1989 Minnesota *Groundwater Protection Act* is to maintain groundwater "in its natural condition, free from degradation caused by human activities" (*Minnesota Statutes*, section 103H.001). However, when groundwater quality monitoring shows degradation has occurred, the *Groundwater Protection Act* authorizes the Minnesota Department of Health (MDH) to develop and establish into rule health-protective limits, known as Health Risk Limits (HRLs), for contaminants found in groundwater that may be used for drinking purposes (*Minnesota Statutes*, section 103H.201. An HRL is a concentration of a groundwater contaminant, or a mixture of contaminants that can be consumed with little or no risk to health, and which has been promulgated under rule. It is expressed as micrograms of a chemical per liter of water (µg/L). MDH calculates HRL values for specific durations of exposure.

MDH proposes to amend the existing rules on Health Risk Limits for Groundwater (henceforth, HRL rules) (*Minnesota Rules*, Chapter 4717, part 7860 and part 7500) in 2010. No other parts of the HRL rules are being amended. The proposed amendments will add HRL values for 14 groundwater contaminants and repeal outdated HRL values (see Section II) from the current rules. The proposed amendments build on MDH's 2009 rule revision, which significantly revised the HRL rules (*Minnesota Rules*, parts 4717.7810 to 4717.7900).[1] Details on the 2009 HRL rule revision are presented in Section I.

In keeping with the *Minnesota Administrative Procedure Act* (APA) (*Minnesota Statutes*, section 14.131), MDH is required to justify the need to amend the existing HRL rules and the reasonableness of the amendments in a Statement of Need and Reasonableness (SONAR). This document fulfills that requirement.

This SONAR is divided into four sections. Section I includes MDH's statutory authority to adopt HRL rules and past MDH rule revisions. MDH defines the concept of HRLs and summarizes the methods MDH used to derive the HRL values. Section II includes the scope of the amendments MDH proposes in 2010. Section III includes an explanation of each provision in the proposed 2010 rules. Section IV includes a discussion of the

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[1] The rules on the Health Risk Limits for Groundwater (*Minnesota Rules,* Chapter 4717, various parts) are available on the Minnesota Department of Health's website at http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlrule.html.
The rules on Health Risk Limits for Groundwater (*Minnesota Rules,* Chapter 4717, various parts) are also available on the Minnesota Office of the Revisor of Statutes' website at: https://www.revisor.mn.gov/rules/?id=4717

regulatory factors and presents information on the performance-based rules, the additional notice plan and the impact of the proposed rules as required per *Minnesota Statutes*, section 14.131.

I. Background

This section presents background information on MDH's guidance on groundwater contaminants. MDH describes the statutory authority to review, derive, promulgate and revise HRL values; provides historical information about MDH's past rule revisions; defines HRL values; and summarizes the methods MDH used to derive HRL values. Note: Detailed description of the methods and the underlying principles are documented in MDH's 2008 SONAR (MDH, 2008. See Part IV, page 21 and following).[2]

A. Statutory Authority

1. THE GROUNDWATER PROTECTION ACT, 1989

MDH derives its statutory authority to promulgate HRLs from the *Groundwater Protection Act* of 1989 (the 1989 Act) (*Minnesota Statutes*, section 103H.201, subd. (1)(a)). The 1989 Act states:

> "If groundwater quality monitoring results show that there is a degradation of groundwater, the commissioner of health may promulgate health risk limits under subdivision 2 for substances degrading the groundwater."

The 1989 Act defines an HRL as (*Minnesota Statutes*, section 103H.005, subd. (3)):

"a concentration of a substance or chemical adopted by rule of the commissioner of health that is a potential drinking water contaminant because of a systemic or carcinogenic toxicological result from consumption."

The authority to adopt HRLs is stated in *Minnesota Statutes*, section 103H.201, subd. (2)(a):

"(a) Health risk limits shall be adopted by rule."

The methods to derive HRLs are specified in *Minnesota Statutes*, section 103H.201, subd. (1)(c) and (d):

> "(c) For systemic toxicants that are not carcinogens, the adopted health risk limits shall be derived using United States Environmental Protection Agency risk assessment methods using a reference dose, a drinking water equivalent, and a relative source contribution factor.

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[2] MDH's 2008 SONAR is available at:
http://www.health.state.mn.us/divs/eh/risk/rules/water/hrlsonar08.pdf

(d) For toxicants that are known or probable carcinogens, the adopted health risk limits shall be derived from a quantitative estimate of the chemical's carcinogenic potency published by the United States Environmental Protection Agency and determined by the commissioner to have undergone thorough scientific review."

MDH's authority to review and revise HRLs is stated in *Minnesota Statutes*, section 103H.201, subd. (3)(a) and (b):

"(a) The commissioner shall review each adopted health risk limit at least every four years.

(b) The commissioner may revise health risk limits under subdivision 2."

2. HEALTH STANDARDS STATUTE, 2001

Additional authority is implicit under the 2001 *Health Standards Statute* (*Minnesota Statutes*, section 144.0751) applicable to safe drinking water and air quality standards. Per this provision, safe drinking water standards must:

"(1) be based on scientifically acceptable, peer-reviewed information; and

(2) include a reasonable margin of safety to adequately protect the health of infants, children, and adults by taking into consideration risks to each of the following health outcomes: reproductive development and function, respiratory function, immunologic suppression or hypersensitization, development of the brain and nervous system, endocrine (hormonal) function, cancer, general infant and child development, and any other important health outcomes identified by the commissioner."

Under the provisions cited above, in cases of groundwater degradation, MDH has the authority to review, develop and promulgate HRLs for groundwater contaminants based on scientific methods to protect sensitive populations.

B. Past MDH Rule Revisions

The MDH Division of Environmental Health has been providing health-based guidance on drinking water contaminants since the mid-1970s. MDH does not enforce or regulate the use of health-based guidance but provides recommended values for use by risk assessors and risk managers in making decisions and evaluating health risks. MDH health-based guidance is only one set of criteria that state groundwater and environmental protection programs use to evaluate contamination. The earliest guidance that MDH developed was the Drinking Water Recommended Allowable Limits (RALs). A RAL was defined as a concentration of a contaminant in water that is protective of human health. RALs were primarily developed for private water supplies,

but were also used for public water supplies in the absence of applicable federal standards.

The 1989 Act authorized MDH to promulgate HRLs for contaminants found in Minnesota groundwater. In 1993, MDH promulgated methods to calculate HRLs and adopted HRL values for chemicals based on those methods. In 1994, additional HRL values were promulgated based 1993 methods (henceforth, referred to as 1993-1994 HRL values).

In 2001, MDH toxicologists and risk assessors evaluated the adequacy of the 1993 methods to calculate the HRL values. Central to the review effort was the intent to:

- Provide guidance on new contaminants found in Minnesota groundwater;
- Update existing HRL values with new toxicological research and exposure data;
- Incorporate advances in risk assessment methods;
- Reflect changes in values and policies regarding children's environmental health; and
- Respond to the directive in the 2001 *Health Standards Statute* (*Minnesota Statutes*, section 144.0751) to protect sensitive subpopulations such as pregnant women and infants.

The review spanned seven years during which MDH hosted public meetings and invited stakeholder participation. MDH also convened subject-matter expert reviews of the methods to establish an updated risk algorithm to derive HRLs and corresponding policies. MDH began formal rulemaking in 2008 by proposing an updated methodology to derive HRL values based on the Environmental Protection Agency's (EPA) risk assessment guidelines (see Section I.D). In 2009, MDH adopted the new methods and the HRL values for 21 groundwater contaminants that were derived using the updated methodology. *Minnesota Rules*, Chapter 4717, parts 4717.7100 through 4717.7800 were repealed (except part 4717.7500) and revised rules as parts 4717.7810 through 4717.7900 were adopted. Additional details on the nature and scope of MDH's 2009 HRL rule revision are documented in the 2008 SONAR (MDH, 2008).

C. Defining Health Risk Limits (HRLs)

HRLs are a type of health-protective guidance developed by MDH for groundwater contaminants that pose a potential threat to human health if used for drinking purposes. The 1989 Act (*Minnesota Statutes*, section 103H.005, subd. (3)) defines an HRL as:

> "…a concentration of a substance or chemical adopted by rule of the commissioner of health that is a potential drinking water contaminant because of a systemic or carcinogenic toxicological result from consumption."

As previously stated, MDH defines an HRL as a concentration of a groundwater contaminant, or a mixture of contaminants that can be consumed with little or no risk to health, and which has been promulgated under rule. MDH calculates HRL values for specific durations of exposure. An HRL is expressed as micrograms of a chemical per liter of water (µg/L).

MDH develops and adopts HRLs for substances or chemicals that contaminate groundwater as a result of human activities (*Minnesota Statutes*, sections 103H.201 and 103H.005, subd. (6)). In deriving HRLs, MDH evaluates contaminant levels as though the groundwater were used for drinking purposes. This is consistent with the declaration in *Minnesota Statutes*, section 115.063, subd. (2) that the "actual or potential use of the waters of the state for potable water supply is the highest priority use" and with the stated statutory intent to prevent degradation (*Minnesota Statutes*, sections 103H.001) and to protect groundwater (*Minnesota Statutes*, section 115.063, subd. (1)).

Risk managers in partner state agencies such as the Minnesota Department of Agriculture (MDA) and the Minnesota Pollution Control Agency (MPCA) use HRLs in their risk abatement and contamination response programs. In addition, MDH's Site Assessment and Consultation Unit (SAC), the Drinking Water Protection and Well Management programs use HRLs.

Except for the requirements for water resources protection (specified in *Minnesota Statutes*, section 103H.275, subd. (1)(c)(2)), neither the 1989 Act nor the current HRL rules (*Minnesota Rules*, Chapter 4717) specifies how HRLs should be used. In issuing guidance, MDH assumes risk managers consider several principles when applying HRLs. MDH-derived HRLs:

- Specify a water quality level acceptable for human consumption;
- Should not be interpreted as acceptable degradation levels;
- Do not address non-ingestion pathways of exposure to contaminants in water (e.g., dermal or inhalation), except in apportioning exposure through the use of a Relative Source Concentration (RSC) factor (for more information on RSC, see MDH, 2008 {Part IV.E.1, page 51} and *Minnesota Rules*, part 4717. 7820, subp. 22);
- Do not account for economic or technological factors such as the cost or feasibility of treatment; and
- Do not account for the potential impact on the environment outside the realm of drinking water, or the health of non-human species.

MDH cannot anticipate all the situations in which HRLs might provide meaningful guidance. Nor can MDH anticipate all the factors that might determine whether the application of an HRL is appropriate. As mentioned before, HRLs are but one of several sets of criteria that state groundwater, drinking water, and environmental protection programs may use to evaluate water contamination. Each program must determine

whether to apply an HRL or whether site-specific characteristics justify deviation from HRLs.

D. MDH-derived Health Risk Limit (HRL) Algorithm

As stated previously, MDH derives HRL values using the methods MDH promulgated in 2009 (*Minnesota Rules,* parts 4717.7810 through 4717.7900). The calculation used to develop an HRL value is a function of how toxic a chemical is (that is, the minimum quantity that will cause health effects), the duration of exposure, and the amount of water individuals drink (intake rates) during the exposure period.

The MDH approach for developing non-cancer HRL values (nHRL) for effects other than cancer is specified in statute (*Minnesota Rules,* part 4717.7830, subp. 2). MDH also uses this approach for chemicals that have effects other than cancer and for chemicals that cause cancer only after a known dose level is exceeded (e.g., threshold carcinogens). The risk algorithm used to derive nHRL values is:

$$nHRL_{duration} = \frac{RfD_{duration} \times RSC \times 1{,}000}{IR_{duration}}$$

Where:

$nHRL_{duration}$ = the non-cancer health risk limit (nHRL), for a given duration, expressed in units of micrograms of a chemical per liter of water (µg/L) (*Minnesota Rules*, part 4717.7820, subp. 13).

$RfD_{duration}$ = the reference dose (RfD) for a given duration, expressed in units of milligrams per kilogram per day (mg/kg-day). The following default durations are used: (i) acute – a period of 24 hours or less; (ii) short-term – a period of more than 24 hours, up to 30 days; (iii) subchronic – a period of more than 30 days, up to approximately 10% of the life span in humans; or (iv) chronic – a period of more than approximately 10% of the life span in humans (*Minnesota Rules*, part 4717.7820, subp. 9 and 21).

RSC = the relative source contribution (RSC) factor which represents the percentage of total exposure to a substance or chemical that is allocated to ingestion of water. The default RSC is 20 percent (0.2) for highly volatile chemicals. For other chemicals, the default RSC is 50 percent (0.5) for acute and short-term HRLs and 20 percent (0.2) for subchronic or chronic HRLs (*Minnesota Rules*, part 4717.7820, subp. 22).

1,000 = a factor used to convert milligrams (mg) to micrograms (µg) (*Minnesota Rules*, part 4717.7830, subp. 2, item D).

$IR_{duration}$ = the intake rate (IR) of ingestion of water, or simply the amount of water, on a per body weight basis, ingested on a daily basis (liters per kg body weight per day or L/kg-day). The default IR corresponds to the time-weighted average (TWA) of the 95th

> percentile intake rate during the relevant duration: acute and short-term - 0.289 L/kg-day, based on intake for 1 up to 3 months of age; subchronic - 0.077 L/kg-day, based on a TWA up to 8 years of age; and chronic - 0.043 L/kg-day, based on a TWA over a lifetime of approximately 70 years (*Minnesota Rules*, part 4717.7820, subp. 14).

Additional explanations of the concepts used in deriving the HRLs are available in Appendix C of this SONAR and in MDH's 2008 SONAR (MDH, 2008. See Part IV).

MDH departed from the above default HRL algorithm and parameter values if sufficient chemical-specific information indicated that a different duration or intake rate was more appropriate. In these cases, a time-weighted intake rate was calculated over the duration specified by the chemical-specific information. The RfD, RSC and IR values used in deriving each nHRL for chemicals included in the 2010 proposed rules are presented in Section III.B.

As indicated in the risk algorithm, the magnitude of the HRL value is a function of the RfD and the IR. In general, for a given chemical, the shorter-duration RfD values will be higher than the longer-duration RfD values because the human body can usually tolerate a higher dose when the duration of the dose is short, even if that same dose would be harmful when it occurs over a longer duration. In most cases, therefore, the calculated HRL values decrease with increasing duration, e.g., acute HRLs are greater than short-term HRLs; short-term HRLs are greater than subchronic HRLs, and so on. It is possible, however, that the RfD for a shorter duration is similar to, or in rare cases lower, than the RfD for a longer duration. This could occur for various reasons such as if a short duration was sufficient to elicit the same adverse effect found in longer-duration study; or if the health effect assessed only in the shorter-duration study occurred at a lower dose than the effect assessed in the longer-duration study; or if the life stage or species assessed only in the shorter-duration study was more sensitive to the toxicant than the life stage or species assessed in the longer-duration study.

The intake rate also affects the magnitude of the HRL value. As described above, the shorter-duration intake rates are higher than the longer-term intake rates. These higher intake rates combined with the RfD may produce a shorter-duration HRL that is less than the calculated longer-duration HRL. When this occurs, the longer-duration HRL is set equal to the lower, shorter-duration HRL. This ensures that the HRL for a longer duration is protective of higher shorter-term intakes that occur within the longer-duration. In instances where the calculated longer-duration HRL value is set at the shorter-duration HRL value, the health endpoints identified will include the health endpoints specified for the shorter-duration, and may include additional health endpoints. These additional health endpoints are included if they are associated with

longer-duration exposure to drinking water concentrations similar in magnitude to the shorter-duration HRL.

In accordance with the general rule for calculations involving multiplication or division, HRLs are rounded to the same number of significant figures as the least precise parameter used in their calculation (EPA 2000c). As a result, the HRL values are rounded to one significant figure. MDH rounded the values as the final step in the calculation (see chemical-specific summary sheets in Appendix E).

II. 2010 Proposed Rules

This section describes the scope of the proposed rules and the basis for contaminants considered in the amendments.

A. Scope

The 2010 proposed rules build on the 2009 HRL rule revision. The proposed revisions are limited to *Minnesota Rules*, part 4717.7860 and part 4717.7500 as noted below. No other parts of the HRL rules are being amended. Through the proposed rules, MDH intends to:

- Promulgate HRL values for 14 additional groundwater contaminants developed using the 2009 methodology. The proposed HRL values will be appended to *Minnesota Rules*, part 4717.7860 (see Section III.B. for details); and
- Repeal outdated guidance for 27 contaminants adopted in 1993-1994 from *Minnesota Rules*, part 4717.7500 (see Section III. C. for details).

B. Selection of Contaminants for Review

MDH selected the contaminants for the 2010 amendments based on input from partner agencies such as the MPCA and the MDA. The agencies expressed a need for guidance on contaminants that might be of emerging concern and those that are commonly detected by the agencies in their monitoring and remediation efforts. The agencies also asked for guidance that incorporates current scientific risk assessment principles.

At past interagency meetings (held on August 23, 2007 and May 8, 2008), representatives from these agencies nominated chemicals for review, discussed their concerns about specific contaminants, and ranked a list of chemicals according to the agency's need for guidance. Through consensus, the collaborating agencies developed a final list of priority chemicals. MDH drew from this list to create a work plan and assessed 14 chemicals (see Appendix D) for health risks and issue guidance. As MDH reviewed each chemical, the following information was posted on MDH's Chemicals Under Review[3] webpage—the chemical's name, its Chemical Abstracts Service (CAS) number, and the

[3] The Chemicals Under Review webpage is available at: http://www.health.state.mn.us/divs/eh/risk/review/index.html

date it was posted. Upon completion of each review, MDH posted the guidance values and the chemical-specific summary sheets on the Groundwater Values Table[4] webpage. MDH also notified those subscribed to the MDH groundwater rules and guidance e-mail notification service about the availability of updated guidance.

C. Application of MDH-derived Methods

The proposed MDH HRLs are derived using the methods promulgated in 2009. The 2009 methods reflect current scientific risk assessment principles; therefore, MDH *is not* proposing any changes to these methods in the 2010 proposed amendments.

MDH methods can be used to derive HRLs for both carcinogens and noncarcinogens. The scientific community now recognizes that cancer-causing chemicals can be assessed in two ways, depending on the way that the chemical causes cancer. Many carcinogens exhibit a non-linear dose response relationship in studies of toxicity, and a dose can be identified at which cancer will not develop (i.e. a threshold). For these contaminants, HRLs are based on the methodology for systemic toxicants rather than the methodology using carcinogenic potency described in the 2008 SONAR (MDH, 2008) for linear (non-threshold) carcinogens. In the 2010 proposed HRL amendments, there is one "threshold" carcinogen, metolachlor. There are no proposed HRLs in this amendment that are based on a linear dose-response.

D. Selection of Contaminants to be Repealed

Since 2008, MDH determined that the HRL values for 27 of the 1993-1994 HRL contaminants listed in *Minnesota Rules*, part 4717.7500 are outdated. MDH is repealing this outdated guidance. Of the 27 contaminants reviewed, updated guidance was promulgated for 15 contaminants in MDH's 2009 rule revision; the 2010 proposed rules include updated HRL values for 8 contaminants; and MDH has issued alternate public heath-protective guidance for the remaining 4 contaminants.

III. Rule-by-Rule Analysis

This section explains the Health Risk Limits Table (*Minnesota Rules*, part 4717.7860) and discusses each provision of the rules proposed by MDH. It also lists the chemicals MDH proposes to repeal from part 4717.7500.

A. EXPLAINING THE HEALTH RISK LIMITS TABLE (Minnesota Rules, part 4717.7860)

The Health Risk Limits table in *Minnesota Rules*, part 4717.7860 lists the HRL values derived for chemicals found in Minnesota's groundwater. As noted before, an HRL

[4] The Groundwater Values Table is available at:
http://www.health.state.mn.us/divs/eh/risk/guidance/gw/table.html

represents the health-protective limit of the concentration of a contaminant in groundwater that poses little or no risk to human health, including vulnerable subpopulations, based on current scientific knowledge. HRL values are derived using the methodology specified in *Minnesota Rules*, parts 4717.7830 and 4717.7840 of existing HRL rules.

For each of the chemicals and their proposed HRL values, the following information is provided: the chemical name; the CAS Registry Number that uniquely identifies each chemical; the year the chemical's HRL value is proposed to be established into rule; and the chemical's volatility classification (low, moderate or high). HRL values are derived for different durations of exposure (acute, short-term, subchronic, chronic and cancer). Also noted are duration-specific RfD, RSC, and default water IR. Adverse health impacts from exposures to contaminants over the range of durations are also noted. Health endpoints refer to the organ system within which the most sensitive adverse effect(s) was observed. Additional explanation of these terms is available in Appendix C.

Notes

- MDH used the following default RSC values—for highly volatile contaminants, the RSC is 20 percent (0.2) for all exposure durations. For chemicals that are not highly volatile, the RSC is 50 percent (0.5) for durations that utilize the intake rate for young infants or 20 percent (0.2) for all other exposure durations.
- The RfDs and uncertainty adjustments are derived by MDH, unless otherwise noted. The RfDs and the endpoints are based on animal studies.
- A health endpoint designation of "none" is used when a general adverse effect (e.g. decreased body weight) cannot be attributed to a specific organ system.
- The duration-specific non-cancer HRL value is derived using the following equation as previously stated in Section I.D and specified in *Minnesota Rules*, part 4717.7830, subp 2:

$$nHRL_{duration} = \frac{(RfD) \times (RSC) \times (Conversion\ Factor)}{(IR_{duration}, L/kg/d)}$$

Example 1 below shows the derivation of the short-term non-cancer HRL value for acetochlor ESA:

$$\text{Short-term Non-cancer HRL} = \frac{(0.37\ mg/kg/d) \times (0.5\ ) \times (1000\ \mu g/mg)}{(0.289\ L/kg\text{-}d)}$$

$$= 640 \text{ rounded to } 600\ \mu g/L$$

The following example explains cases where the calculated non-cancer HRL for a longer-duration period is set to a shorter-duration HRL value to be protective of

shorter-term exposures that occur during the reference period (see Section III.B for more details).
Example 2 below shows the derivation of the subchronic non-cancer HRL for ethylbenzene:

$$\text{Subchronic Non-cancer HRL} = \frac{(0.048\ \text{mg/kg/d}) \times (0.2) \times (1000\ \mu\text{g/mg})}{(0.077\ \text{L/kg-d})}$$

$$= 124 \text{ rounded to } 100\ \mu\text{g/L}$$

The calculated subchronic non-cancer HRL (100 μg/L) is greater than ethylbenzene's short-term HRL value of 50 μg/L (see the chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value for ethylbenzene is 50 μg/L. The health endpoints include the hepatic and renal system. So in this case:

$$\text{Subchronic Non-Cancer Health Risk Limit } (nHRL_{subchronic}) = (nHRL_{short\text{-}term}) = 50\ \mu\text{g/L}$$

- The terms used in this section are explained below. Detailed explanations are also available in the Glossary (see Appendix A).
  - Acute, short-term, subchronic and chronic refer to the lengths of exposure periods.
  - HRL refers to the chemical's final health risk limit value for each exposure duration.
  - RfD refers to the reference dose, or an estimate of the daily oral exposure that poses little or no risk for a given exposure duration.
  - RSC refers to the relative source contribution, or the proportion of the individual's total permissible exposure allocated to ingestion of water.
  - SF refers to the slope of a curve that expresses the relation between cancer risk and dose.
  - ADAF refers to the age-dependent adjustment factors of the cancer slope factor to take early-life susceptibility into account for linear (non-threshold) carcinogens.
  - IR refers to the intake rate, or the time-weighted-average rate of ingestion of water per kg of body weight.
  - Endpoints refer to critical or co-critical effects of chemicals when evaluating health risks.

- The symbols that appear in the tables in Section III.B. are explained below:
  - "-" means not relevant

- "NA" means not applicable. "NA" in the cancer column means that the chemical has not been classified as a linear (non-threshold) carcinogen
- "ND" means not derived due to absence or paucity of toxicity information
- "None" means that the HRL value is based on a general adverse effect (e.g. reduced adult body weight) not attributable to a specific organ system and therefore it is not applicable for inclusion in the additivity calculations for the health risk index.
- The following explanations apply where noted in the tables in Section III.B:
    (1) If the calculated HRL value is greater than the acute value, to be protective of acute exposures, the HRL is set to equal the acute HRL value;
    (2) If the calculated HRL value is greater than the short-term HRL value, to be protective of short-term exposures, the HRL is set equal to the short-term HRL value; and
    (3) If the calculated HRL is greater than the subchronic HRL, to be protective of subchronic exposures, the HRL is set to equal the subchronic HRL value.

B. PROPOSED RULES: THE HEALTH RISK LIMITS TABLE (Minnesota Rules, part 4717.7860)

Subpart 3a. Acetochlor ESA (degradate of the parent compound, acetochlor)

CAS number: 187022-11-3
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 600 µg/L. The RfD is 0.37 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variability, 3 for minimal LOAEL-to-NOAEL, and 3 for database insufficiencies due to a lack of multigenerational reproductive studies or developmental studies). The point of departure LOAEL is 370.3 mg/kg-day based on increased levels of the thyroid stimulating hormone (TSH) and free thyroxine (T4) in animal studies.

Subchronic duration.
The subchronic non-cancer proposed HRL is 600 µg/L. The RfD is 0.23 mg/kg-day, the RSC is 0.2 and the intake rate of 0.077 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variability, and 10 for database

insufficiency {lack of multigenerational reproductive or developmental studies, insufficient studies for neurological and endocrine effects, and lack of studies in a second species}). The point of departure NOAEL is 255.4 mg/kg-day based on decreased food utilization and decreased body weight and body weight gain in animal studies. Co-critical effects include alterations in serum thyroid hormone.

Chronic duration.
The chronic non-cancer proposed HRL is 300 µg/L. The RfD is 0.075 mg/kg-day, the RSC is 0.2 and the intake rate of 0.043 L/kg-day. The total uncertainty adjustment is 3,000 (10 for inter species extrapolation, 10 for intra species variability, 10 for database insufficiencies {lack of multigenerational reproductive or developmental studies, insufficient neurological and endocrine effects, and lack of studies in second species}, and 3 for use of a subchronic study. The point of departure NOAEL is 225.4 mg/kg-day based on decreased food utilization and decreased body weight and body weight gain in animal studies. Co-critical effects include alterations in serum thyroid hormone.

Cancer.
Not applicable. Acetochlor ESA's carcinogenic potential has not been classified. However, the EPA indicates that it is unlikely to be a carcinogen. The parent compound, acetochlor, is classified as a "likely" nonlinear (threshold) carcinogen (*Minnesota Rules*, part 4717.7860, subp. 3).

Table 1 : Acetochlor ESA

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (µg/L)	ND	600	600	300	NA
RFD (mg/kg-day)	--	0.37	0.23	0.075	--
RSC	--	0.5	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	0.077	0.043	--
Endpoints	--	Thyroid (E)	Thyroid (E)	Thyroid (E)	--

Subpart 3b. Acetochlor OXA (degradate of the parent compound, acetochlor)

CAS number: 184992-44-4
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 200 μg/L. The RfD is 0.12 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 3,000 (10 for inter species extrapolation, 10 for intra species variability, 10 for LOAEL-to-NOAEL, and 3 for database insufficiency (lack of multigenerational reproductive study). The point of departure LOAEL is 370 mg/kg-day based on decreased body weight gain, changes in thyroid hormone levels and increased relative thyroid weight in animal studies.

Subchronic duration.
The subchronic non-cancer HRL is 200 μg/L. The RfD is 0.077 mg/kg-day and the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency {lack of multigenerational reproductive study, insufficient studies for neurological and endocrine effects, and lack of studies in a second species}). The point of departure NOAEL is 77.2 mg/kg-day based on decreased food utilization, body weight and body weight gain in animal studies. Co-critical effects for this duration include alterations in serum thyroid levels.

Chronic duration.
The chronic non-cancer HRL is 100 μg/L. The RfD is 0.026 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 3,000 (10 for inter species extrapolation, 10 for intra species variability and 10 for database insufficiencies {lack of multigenerational reproductive or developmental studies, insufficient neurological and endocrine effects, and lack of studies in second species} and 3 for use of a subchronic study). The point of departure NOAEL is 77.2 mg/kg-day based on decreased food utilization, body weight and body weight gain in animal studies. Co-critical effects for this duration include alterations in serum thyroid levels.

Cancer.
Not applicable. Acetochlor OXA's carcinogenic potential has not been classified. However, the EPA indicates that it is unlikely to be a carcinogen. The parent compound, acetochlor, is classified as a "likely" nonlinear carcinogen.

Table 2 : Acetochlor OXA

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	200	200	100	NA
RFD (mg/kg-day)	--	0.12	0.077	0.026	--
RSC	--	0.5	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	0.077	0.043	--
Endpoints	--	Thyroid (E)	Thyroid (E)	Thyroid (E)	--

Subp. 3c. Acetone

CAS number: 67-64-1
Year Proposed: 2010
Volatility: Moderate

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 9,000 μg/L. The RfD is 5.0 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 300 (10 for inter species variability, 3 for toxicokinetic differences {the toxicodynamics component is 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic effects of acetone. Studies show that humans and rodents metabolize acetone at low doses in the liver and by extrahepatic pathway followed by excretion at a higher concentration}, 10 for database insufficiencies {lack of multigenerational studies and inadequate oral neurotoxicity, and lack of developmental and neurotoxicity studies}). The point of departure NOAEL is 1,485 mg/kg-day based on increased kidney weight in animal studies.

Subchronic duration.
The subchronic non-cancer proposed HRL is 8,000 μg/L. The RfD is 3.0 mg/kg-day, the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 300 (10 for inter species extrapolation, 10 for intra species variation, 3 for toxicokinetic differences {the toxicodynamics component is 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic effects of acetone. Studies show that

humans and rodents metabolize acetone at low doses in the liver and by extrahepatic pathway followed by excretion at a higher concentration}, 10 for database insufficiencies {lack of multigenerational studies and inadequate oral neurotoxicity, and lack of developmental and neurotoxicity studies.}) The point of departure NOAEL is 900 mg/kg-day based on nephropathy (renal system) and changes in the hematological (blood) parameters consistent with bone marrow toxicity in animal studies. Co-critical effects include tubular degeneration of kidneys.

Chronic duration.
The chronic non-cancer proposed HRL is 4,000 μg/L. The RfD is 0.9 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variation, 3 for toxicokinetic differences {the toxicodynamics component is 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic effects of acetone. Studies show that humans and rodents metabolize acetone at low doses in the liver and by extrahepatic pathway followed by excretion at a higher concentration}, 10 for database insufficiencies {lack of multigenerational studies and inadequate oral neurotoxicity, and lack of developmental and neurotoxicity studies}, and a subchronic-to-chronic uncertainty factor of 3 is used due to uncertainty about increased severity of effects from increased duration of oral exposure to acetone.) The source of RfD and the uncertainty factor allocation is the same as that developed by the EPA. The point of departure NOAEL is 900 mg/kg-day based on nephropathy (renal system) and changes in the hematological (blood) parameters consistent with bone marrow toxicity in animal studies. Co-critical effects include tubular degeneration of kidneys.

Cancer.
Not applicable. No cancer classification is available for acetone.

Table 3 : Acetone

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	9,000	8,000	4,000	NA
RFD (mg/kg-day)	--	5.0	3.0	0.90	--
RSC	--	0.5	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	0.077	0.043	--
Endpoints	--	Renal (kidney) system	Renal (kidney) system,	Renal (kidney) system,	--

			Hematological (blood) system	Hematological (blood) system	

Subp. 8a. Dichlorodifluoromethane

CAS number: 75-71-8
Year Proposed: 2010
Volatility: High

Acute duration.
Not derived due to insufficient data.

Short-term duration.
Not derived due to insufficient data.

Subchronic duration.
Not derived due to insufficient data.

Chronic duration.
The chronic non-cancer proposed HRL is 700 µg/L. The RfD is 0.15 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variability, 3 for LOAEL-to-NOAEL, and 3 for database insufficiency {lack of developmental study and detailed study information}). The point of departure LOAEL is 150 mg/kg-day based on decreased body weight.

Cancer.
Not applicable. The human carcinogenicity is not classifiable for Group D chemicals.

Table 4: Dichlorodifluoromethane

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (µg/L)	ND	ND	ND	700	NA
RFD (mg/kg-day)	--	--	--	0.15	--
RSC	--	--	--	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--

Intake Rate (L/kg-day)	--	--	--	0.043	--
Endpoints	--	--	--	None	--

Subp. 8b. 1,1-Dichloroethylene

CAS number: 75-35-4
Year Proposed: 2010
Volatility: High

Acute duration.
Not derived due to insufficient data.

Short-term duration.
Not derived due to insufficient data.

Subchronic duration.
The subchronic non-cancer proposed HRL is 200 μg/L. The RfD is 0.090 mg/kg-day, the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variation). The point of departure NOAEL is 9 mg/kg-day based on fatty changes in the liver in animal studies.

Chronic duration.
The chronic non-cancer proposed HRL is 200μg/L. The RfD is 0.046 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variation). The point of departure $BMDL_{10}$ is 4.6 mg/kg-day based on fatty changes in the liver in animal studies.

Cancer.
Not applicable. For this chemical, the assessment of the human carcinogenic potential by the oral route was inadequate.

Table 5: 1,1-Dichloroethene

	Acute	**Short-term**	**Subchronic**	**Chronic**	**Cancer**
HRL (μg/L)	ND	ND	200	200	NA
RFD (mg/kg-day)	--	--	0.090	0.046	--
RSC	--	--	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--

ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	--	0.077	0.043	--
Endpoints	--	--	Hepatic (liver) system	Hepatic (liver) system	--

Subp. 12a. Ethylbenzene

CAS number: 100-41-4
Year Proposed: 2010
Volatility: High

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 50 μg/L. The RfD is 0.075 mg/kg-day, the RSC is 0.2 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variation and 10 for database deficiencies {lack of oral studies of developmental and reproductive toxicity, lack of toxicity data in more than one specie, and limited evidence of otoxicity that may be relevant to the oral route of exposure}). The point of departure NOAEL is 75 mg/kg-day based on changes to the liver and kidney weights (with histological changes seen at higher doses) in animal studies.

Subchronic duration.
The calculated subchronic non-cancer HRL is greater than the short-term HRL value of 50 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value is 50 μg/L.

Chronic duration.
The calculated chronic non-cancer HRL is greater than the short-term HRL value of 50 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the chronic HRL must be protective of the short-term exposures that occur within the chronic period, the chronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the chronic non-cancer HRL value is 50 μg/L.

Cancer.
Not applicable. The cancer classification is Group D. These chemicals are not classifiable as to their human carcinogenic potential.

Table 6: Ethylbenzene

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	50	50 (2)	50 (2)	NA
RFD (mg/kg-day)	--	0.075	(2)	(2)	--
RSC	--	0.2	(2)	(2)	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	(2)	(2)	--
Endpoints	--	Hepatic (liver) system, Renal (kidney) system	Hepatic (liver) system, Renal (kidney) system	Hepatic (liver) system, Renal (kidney) system	--

Subp. 12b. Ethylene glycol

CAS number: 107-21-1
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
The acute non-cancer proposed HRL is 4,000 μg/L. The RfD is 0.76 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day (the maternal intake rate is used rather than the default rate, see the chemical-specific summary sheets in Appendix E for details). The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure $BMDL_{10}$ is 75.6 mg/kg-day, based on increased incidence of skeletal malformations in animal studies.

Short-term duration.
The short-term non-cancer proposed HRL is 4,000 μg/L. The RfD is 0.76 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day (the maternal intake rate is used rather than the default rate, see the chemical-specific summary sheets in Appendix E for details). The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10

for intra species variability). The point of departure $BMDL_{10}$ is 75.6 mg/kg-day based on increased incidence of skeletal malformations in animal studies.

Subchronic duration.
The subchronic non-cancer proposed HRL is 2,000 μg/L. The RfD is 0.72 mg/kg-day, the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure $BMDL_{10}$ is 71.5 mg/kg-day, based on decreased adult body weight and adverse renal (kidney) impacts such as increased water intake, lower urine specific gravities and higher urine volumes in animal studies. Co-critical effects include increased incidence of skeletal malformations.

Chronic duration.
The chronic non-cancer proposed HRL is 2,000 μg/L. The RfD is 0.50 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 300 (10 for inter species extrapolation, 10 for intra species variability, 3 for subchronic-to-chronic uncertainty factor). The point of departure NOAEL is 150 mg/kg-day and the LOAEL is 300 mg/kg-day, based on decreased adult body weight and adverse renal (kidney) impacts such as increased water intake, lower urine specific gravities and higher urine volumes in animal studies. Co-critical effects include increased incidence of skeletal malformations.

Cancer.
Not applicable. There is no cancer classification for ethylene glycol. It has not undergone a complete evaluation and determination for human carcinogenic potential by EPA.

Table 7: Ethylene glycol

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	4,000	4,000	2,000	2,000	NA
RFD (mg/kg-day)	0.76	0.76	0.72	0.50	--
RSC	0.2	0.2	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	0.043	0.043	0.077	0.043	--
Endpoints	Developmental	Developmental	Renal (kidney) system, Developmental	Renal (kidney) system, Developmental	--

Subp. 12c. Metolachlor and s-Metolachlor

CAS number: 51218-45-2; 87392-12-9
Year Proposed: 2010
Volatility: Nonvolatile

Acute and Short-term duration.
The acute and short-term non-cancer proposed HRL is 400 µg/L. The RfD is 0.24 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure NOAEL is 23.5 mg/kg-day based on developmental effects in animal studies.

Subchronic duration.
The subchronic non-cancer proposed HRL is 300 µg/L. The RfD is 0.097 mg/kg-day, the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure NOAEL is 9.7 mg/kg-day, based on decreased body weight in adults in animal studies.

Chronic duration.
The calculated chronic non-caner HRL is greater than the subchronic HRL value of 300 µg/L (see chemical-specific summary sheets in Appendix E for details). Since the chronic HRL must be protective of the subchronic exposures that occur within the chronic period, the chronic non-cancer HRL is set equal to the subchronic non-cancer HRL value. Hence, the chronic non-cancer HRL value is 300 µg/L.

Cancer.
Not applicable. This chemical is a "possible human carcinogen" (Class C) as classified by the EPA.

Table 8: Metolachlor and s- metolachlor

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (µg/L)	400	400	300	300 (3)	NA
RFD (mg/kg-day)	0.24	0.24	0.097	(3)	--
RSC	0.5	0.5	0.2	(3)	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--

Intake Rate (L/kg-day)	0.289	0.289	0.077	(3)	--
Endpoints	Developmental	Developmental	None	None	--

Subp. 12d. Metolachlor ESA

CAS number: 171118-09-5
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
Not derived due to insufficient data.

Subchronic duration.
The subchronic non-cancer proposed HRL is 4,000 μg/L. The RfD is 1.7 mg/kg-day, the RSC is 0.2 and the intake rate is 0.077 L/kg-day. The total uncertainty adjustment is 300 (10 for inter species extrapolation, 10 for intra species variability and 3 for database insufficiencies {lack of a two-generation reproductive study}). The point of departure NOAEL is 500 mg/kg-day, based on increased levels of serum liver enzymes and liver weight in animal studies.

Chronic duration.
The chronic non-cancer proposed HRL is 800 μg/L. The RfD is 0.17 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 3,000 (10 for inter species extrapolation, 10 for intra species variability, 10 for use of a subchronic study and 3 for database insufficiencies {lack of a two-generation reproductive study}). The point of departure NOAEL is 500 mg/kg-day, based on increased levels of serum liver enzymes and liver weight in animal studies.

Cancer.
Not applicable. No cancer classification available.

Table 9: Metolachlor ESA

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	ND	4,000	800	NA
RFD (mg/kg-day)	--	--	1.7	0.17	--
RSC	--	--	0.2	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	--	0.077	0.043	--
Endpoints	--	--	Hepatic (liver) system	Hepatic (liver) system	--

Subp. 12e. Metolachlor OXA

CAS number: 152019-73-3
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 3,000 μg/L. The RfD is 1.7 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 300 (10 for inter species extrapolation, 10 for intra species variability and 3 for database insufficiencies {lack of a two-generation reproductive study}). The point of departure NOAEL is 500 mg/kg-day, based on changes in blood chemistry with no specific targeted organ in animal studies.

Subchronic duration.
The calculated subchronic non-cancer HRL is greater than the short-term HRL value of 3,000 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value is 3,000 μg/L.

Chronic duration.
The subchronic non-cancer proposed HRL is 800 µg/L. The RfD is 0.17 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 3,000 (10 for inter species extrapolation, 10 for intra species variability, 10 for use of a subchronic study and 3 for database insufficiencies {lack of a two-generation reproductive study}). The point of departure NOAEL is 500 mg/kg-day, based on changes in blood chemistry with no specific targeted organ in animal studies.

Cancer.
Not applicable. No cancer classification available.

Table 10: Metolachlor OXA

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (µg/L)	ND	3,000	3,000 (2)	800	NA
RFD (mg/kg-day)	--	1.7	(2)	0.17	--
RSC	--	0.5	(2)	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	(2)	0.043	--
Endpoints	--	None	None	None	--

Subp. 14a. Perfluorobutane sulfonate (PFBS)

CAS number: 375-73-5
Year Proposed: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
Not derived due to insufficient data.

Subchronic duration.
The subchronic non-cancer proposed HRL is 9 µg/L. The RfD is 0.0042 mg/kg-day, the RSC is 0.5 and the intake rate is 0.245 L/kg-day (the chemical-specific intake rate is used

rather than the default rate, see the chemical-specific summary sheets in Appendix E for details). The total uncertainty adjustment is 100 (3 inter species extrapolation for potential differences in toxicodynamics, 10 for intra species variability and 3 for database insufficiencies {lack of additional studies on neurological and thyroid effects}). The point of departure NOAEL is 60 mg/kg-day based on decreased hemoglobin and hematocrit and histological changes in the kidneys in animal studies. Co-critical effects include increased liver weight and incidence of hepatocellular hypertrophy.

Chronic duration.
The chronic non-cancer proposed HRL is 7 μg/L. The RfD is 0.0014 mg/kg-day, the RSC is 0.2 and the intake rate is 0.043 L/kg-day. The total uncertainty adjustment is 300 (3 inter species extrapolation for potential differences in toxicodynamics, 10 for intra species variability, 3 for database insufficiencies {lack of additional studies on neurological and thyroid effects} and 3 for using a subchronic study). The point of departure NOAEL is 60 mg/kg-day based on decreased hemoglobin and hematocrit and histological changes in the kidneys in animal studies. Co-critical effects include increased liver weight and incidence of hepatocellular hypertrophy.

Cancer.
Not applicable. No cancer classification available.

Table 11: Perfluorobutane sulfonate (PFBS)

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	ND	9	7	NA
RFD (mg/kg-day)	--	--	0.0042	0.0014	--
RSC	--	--	0.5	0.2	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	--	0.245	0.043	--
Endpoints	--	--	Hepatic (liver) system, Hematological (blood) system, Renal (kidney) system	Hepatic (liver) system, Hematological (blood) system, Renal (kidney) system	--

Subp. 14b. Perfluorobutyrate (PFBA):

CAS number: 375-22-4
Year Established: 2010
Volatility: Nonvolatile

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 7μg/L. The RfD is 0.0038 mg/kg-day, the RSC is 0.5 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 100 (10 for intra species variability, 3 for inter species toxicodynamic differences, and 3 for database insufficiencies {study did not identify a NOAEL or acceptable $BMDL_{10}$ for thyroid effects, lack of a multigenerational reproductive study, although the database does include an extended 1 generation developmental study}). The point of departure $BMDL_{10}$ is 3.01 mg/kg-day, based on decreased cholesterol. Co-critical effects include increased relative thyroid weight and decreased thyroid hormone levels in animal studies.

Subchronic duration.
The calculated subchronic non-cancer HRL is greater than the short-term HRL value of 7μg/L (see chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value is 7 μg/L.

Chronic duration.
The calculated chronic non-cancer HRL is greater than the short-term HRL value of 7μg/L (see chemical-specific summary sheets in Appendix E for details). Since the chronic HRL must be protective of the short-term exposures that occur within the chronic period, the chronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the chronic non-cancer HRL value is 7 μg/L.

Cancer.
Not applicable. No cancer classification available.

Table 12: Perfluorobutyrate (PFBA)

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	7	7 (2)	7 (2)	NA
RFD (mg/kg-day)	--	0.0038	(2)	(2)	--
RSC	--	0.5	(2)	(2)	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	(2)	(2)	--
Endpoints	--	Hepatic (liver) system; Thyroid (E)	Hepatic (liver) system; Thyroid (E)	Hepatic (liver) system; Thyroid (E)	--

Subp. 18a. Toluene:

CAS number: 108-88-3
Year Proposed: 2010
Volatility: High

Acute duration.
Not derived due to insufficient data.

Short-term duration.
The short-term non-cancer proposed HRL is 200 μg/L. The RfD is 0.22 mg/kg-day, the RSC is 0.2 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure NOAEL is 22 mg/kg-day based on immunosuppression in animal studies. Critical effects include changes in brain neurotransmitter levels and nervous system effects.

Subchronic duration.
The calculated subchronic non-cancer HRL is greater than the short-term HRL value of 200 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value is 200 μg/L.

Chronic duration.
The calculated chronic non-cancer HRL is greater than the short-term HRL value of 200 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the chronic HRL must be protective of the short-term exposures that occur within the chronic period, the chronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the chronic non-cancer HRL value is 200 μg/L.

Cancer.
Not applicable. The information available on this chemical is inadequate to classify its carcinogenicity.

Table 13: Toluene

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	ND	200	200 (2)	200 (2)	NA
RFD (mg/kg-day)	--	0.22	(2)	(2)	--
RSC	--	0.2	(2)	(2)	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	--	0.289	(2)	(2)	--
Endpoints	--	Immune system, Nervous system	Immune system, Nervous system	Immune system, Nervous system	--

Subp. 23a. Xylenes:

CAS number: 1330-20-7
Year Established: 2010
Volatility: High

Acute duration.
The acute non-cancer proposed HRL is 800 μg/L. The RfD is 1.2 mg/kg-day, the RSC is 0.2 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 100 (10 for inter species extrapolation and 10 for intra species variability). The point of departure NOAEL is 125 mg/kg-day based on nervous system effects in animal studies.

Short-term duration.
The short-term non-cancer proposed HRL is 300 μg/L. The RfD is 0.5 mg/kg-day, the RSC is 0.2 and the intake rate is 0.289 L/kg-day. The total uncertainty adjustment is 1,000 (10 for inter species extrapolation, 10 for intra species variability, and 10 for database deficiencies {lack of oral multi-generational reproductive, ototoxicity and neurotoxicity studies}). The point of departure NOAEL is 500 mg/kg-day, based on decreased body weight in animal studies. Co-critical effects include nervous system effects.

Subchronic duration.
The calculated subchronic non-cancer HRL is greater than the short-term HRL value of 300 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the subchronic HRL must be protective of the short-term exposures that occur within the subchronic period, the subchronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the subchronic non-cancer HRL value is 300 μg/L.

Chronic duration.
The calculated chronic non-cancer HRL is greater than the short-term HRL value of 300 μg/L (see chemical-specific summary sheets in Appendix E for details). Since the chronic HRL must be protective of the short-term exposures that occur within the chronic period, the chronic non-cancer HRL is set equal to the short-term non-cancer HRL value. Hence, the chronic non-cancer HRL value is 300 μg/L.

Cancer.
Not applicable. No cancer classification available.

Table 14 : Xylenes

	Acute	Short-term	Subchronic	Chronic	Cancer
HRL (μg/L)	800	300	300 (2)	300 (2)	NA
RFD (mg/kg-day)	1.2	0.5	(2)	(2)	--
RSC	0.2	0.2	(2)	(2)	--
SF (per mg/kg-day)	--	--	--	--	--
ADAF or $AF_{lifetime}$	--	--	--	--	--
Intake Rate (L/kg-day)	0.289	0.289	(2)	(2)	--
Endpoints	Nervous system	Nervous system	Renal (kidney) system; Nervous system	Renal (kidney) system; Nervous system	--

C. PROPOSED DELETIONS: THE HEALTH RISK LIMITS TABLE (Minnesota Rules, part *4717.7500)*

Based on MDH's recent review of HRL values for 27 of the contaminants listed in *Minnesota Rules*, part 4717.7500, MDH intends to repeal the outdated guidance promulgated in 1993-1994. Of the 27 contaminants reviewed, updated guidance was promulgated for 15 contaminants in MDH's 2009 rule revision; the 2010 proposed rules include updated HRL values for 8 contaminants; and MDH has issued alternate public heath-protective guidance for the remaining 4 contaminants. The specific subparts to be repealed are noted below:

Table 15: Subparts and chemicals to be repealed from Part 4717.7500

• **3** Acetone	• **52a** Ethylene glycol
• **3a** Alachlor	• **61** Manganese
• **6a** Atrazine	• **65** Metolachlor
• **8** Benzene	• **68** Nitrate (as nitrogen)
• **14** Boron	• **70** Pentachlorophenol
• **25** Chloroform	• **77a** Simazine
• **36** Dichlorodifluoromethane	• **78b** 1,1,2,2-Tetrachloroethylene
• **39a** 1,1-Dichloroethane	• **79** Toulene
• **40a** 1,2-Dichloroethylene (cis)	• **80a** 1,1,1-Trichloroethane
• **41** 1,1-Dichloroethylene (Vinylidene chloride)	• **81a** 1,1,2-Trichloroethylene (TCE)
• **43** Dichloromethane (Methylene chloride)	• **85** 2 (2,4,5-Trichlorophenoxy)propionic acid
• **46** Di(2-ethylhexyl)phthalate (DEHP)	• **88b** Vinyl chloride
• **50** Ethylbenzene	• **89** Xylenes
• **52** Ethyl ether	

IV. REGULATORY ANALYSIS

This section discusses the regulatory factors and presents information on the performance-based rules, the additional notice plan and the impact of the proposed rules, as required by *Minnesota Statutes*, section 14.131.

A. REGULATORY FACTORS

Minnesota Statutes, section 14.131, sets out seven factors for regulatory analysis that must be included in the SONAR. This section discusses each of the factors.

1. CLASSES OF PERSONS PROBABLY AFFECTED BY THE PROPOSED RULE, INCLUDING CLASSES THAT WILL BEAR THE COSTS AND CLASSES THAT WILL BENEFIT

Because these rules address the groundwater Minnesotans rely on for drinking, the proposed amendments could potentially affect all persons living here. Since the application of HRLs falls to the discretion of state agencies charged with protecting

Minnesota's environment and water resources, the best predictor of who will be affected by the rules is to review the way the HRLs are applied.

Generally, the amendments benefit the entire state because HRLs serve as benchmarks in state groundwater monitoring and contamination response programs. The incorporation of HRLs and related chemical data into other state rules intended to protect Minnesota's water resources (e.g., MPCA's solid waste and surface water rules) is also a benefit to the entire state.

More specifically, the amendments can affect individuals or populations when a public or private water supply becomes contaminated and federal Maximum Contaminant Levels (MCLs) are unavailable. In these instances, the responding agency estimates the risks from consuming contaminated water using HRLs, and conveys advice on eliminating or reducing risks to the consumer, the responsible governmental unit, or the water operator. HRLs are the benchmarks most often used to direct monitoring and remediation for pollution control of contaminated groundwater.

The proposed amendments provide protection to life stages that are sensitive or highly exposed. Risk managers have the option of applying HRLs to the general population, or adjusting them for sub-populations.

2. THE PROBABLE COSTS OF IMPLEMENTATION AND ENFORCEMENT AND ANY ANTICIPATED EFFECT ON STATE REVENUES

The proposed amendments *do not* have any direct impact on state revenues. There are no fees associated with the rules, nor are there any specific implementation or enforcement costs. The amendments simply provide health-based levels for certain groundwater contaminants. To the extent that state agencies apply the proposed HRLs, those agencies will have to determine costs on a case-by-case basis.

3. A DETERMINATION OF WHETHER THERE ARE LESS COSTLY OR LESS INTRUSIVE METHODS FOR ACHIEVING THE PURPOSE OF THE PROPOSED RULE, AND A DESCRIPTION OF ALTERNATIVE METHODS CONSIDERED AND REASONS WHY THEY WERE REJECTED

State statutes define the methods by which HRLs are derived and the policy goals they serve. *Minnesota Statutes*, section 103H.201, subd. (1), authorizes the Commissioner of the Department of Health to promulgate HRLs. Methods to be used in deriving HRLs are stated in paragraphs (c) and (d) of subdivision 1. In addition, *Minnesota Statutes*, section 144.0751(a)(1), requires that safe drinking water standards "be based on scientifically acceptable, peer-reviewed information." *Minnesota Statutes*, section 144.0751(a)(2) requires that the standards also "include a reasonable margin of safety to adequately protect the health of infants, children, and adults." In addition to being in statute, these requirements reflect prudent public health policy since groundwater is a primary source of drinking water for Minnesotans, including the very young, the very

old, the sick and the infirm. These statutory mandates provide the boundaries of MDH's discretion in deriving HRLs. Accordingly, MDH derives HRLs using scientific sources and methods that ensure the protection of all Minnesotans. If the agency in charge of a contamination investigation determines that certain groups will not be exposed, that agency can exercise its discretion to apply a different value or manage known and potential risks in other ways.

The MDH-derived HRLs provide uniform, science-based rules that can be applied to the protection of the health of the general public that uses groundwater as a source of drinking water. The MDH-derived HRLs have been derived through a process designed to inform and engage the public.

In addition to the HRLs, MDH derives another type of quantitative guidance on groundwater contaminants as requested by partner state agencies on a case-by-case basis. This guidance, known as Health-Based Values (HBVs), is derived using the same methodology as the HRLs. Because HBVs are unpromulgated, state agencies and the regulated community consider them to be transient in nature as compared to the HRLs, which are considered more permanent and therefore, more useful in planning long-term risk management strategies. The promulgation of the guidance into rule standardizes the use of guidance statewide, and provides the authority and uniformity of rule.

These rules represent the soundest calculations that MDH can supply to fulfill its mission without unduly restricting the parties who ultimately must observe them.

4. A DESCRIPTION OF ANY ALTERNATIVE METHODS FOR ACHIEVING THE PURPOSE OF THE PROPOSED RULE THAT WERE SERIOUSLY CONSIDERED BY THE AGENCY AND THE REASONS WHY THEY WERE REJECTED IN FAVOR OF THE PROPOSED RULE

See above. This factor is combined and addressed with factor 3 (above).

5. THE PROBABLE COSTS OF COMPLYING WITH THE PROPOSED RULE

Because the HRL rules do not specify how the health-protective numbers are to be applied, the probable cost of complying with the proposed amendments cannot be estimated. HRLs are only one set of criteria used to evaluate whether the concentration of a contaminant found in groundwater is associated with a risk to health.
HRLs are not intended to be bright lines between "acceptable" and "unacceptable" concentrations. As previously stated, MDH derives HRLs using conservative methods so that exposures below an HRL would be expected to present minimal if any risk to human health. Similarly, a contaminant concentration above an HRL, without consideration of other information, may not necessarily indicate a public health problem. However, as the proposed HRL values for five chemicals are lower than the 1993/1994 values (dichlorodifluoromethane, ethylbenzene, ethylene glycol, toluene, and xylenes), the cost of remediating or preventing water contamination may increase. On

the other hand, the proposed HRL values for three chemicals in the revised rules are higher than the 1993/94 values (acetone, 1,1-dichloroethene and metolachlor) and therefore, the cost may decrease. The proposed HRL values for six chemicals represent new HRL values. Any costs associated with these are indeterminate.

6. THE PROBABLE COSTS OR CONSEQUENCES OF NOT ADOPTING THE PROPOSED RULE

The probable costs or consequences of not adopting the proposed amendments are immeasurable in terms of effects on groundwater. As stated above, groundwater is a primary source of drinking water for Minnesota, making the need to protect it obvious and imperative.

Though the state's goal is to prevent degradation of groundwater, degradation prevention is the ideal and thus cannot always be achieved. Some groundwater resources have already been contaminated by unintentional releases—by activities that occurred before the vulnerability of groundwater to contamination was known; by activities that occurred before certain chemicals were identified as toxic; or before regulations prohibiting releases had been implemented. HRLs allow authorities to evaluate groundwater to ensure that there is minimal risk to human health from using the groundwater for drinking water. A reliable source of groundwater that is safe for human consumption is essential to the ability of a state to safeguard a high standard of living for its citizens. A failure to revise the rules would ignore legislative directives and leave in place an outdated set of standards that provide only limited protections to segments of the population.

7. DIFFERENCES BETWEEN THE PROPOSED RULE AND EXISTING FEDERAL REGULATIONS, AND THE NEED FOR AND REASONABLENESS OF EACH DIFFERENCE

EPA's Office of Water publishes several sets of drinking water-related standards and health advisories such as Maximum Contaminant Level Goals, Maximum Contaminant Levels, Drinking Water Equivalent Levels, and lifetime Health Advisories. While these are similar to MDH-derived HRLs in some respects, they differ in important ways noted below. Furthermore, for any given chemical, all, several, one, or none of these standards and advisories may have been developed.

MDH-derived HRLs differ from existing federal regulations and advisory values in three primary ways:

- HRLs are based strictly on human health;
- HRLs provide guidance for both cancer and non-cancer effects; and
- The derivation of HRLs explicitly includes a reasonable margin of safety for vulnerable sub-populations such as infants and children, who are considered to potentially be at higher risk than adults.

While some federal regulations or advisory values might adhere to one or two of these conditions, none adheres to all conditions.

EPA-derived Maximum Contaminant Level Goals (MCLGs) are advisory values based solely on considerations of human health. However, by definition, the MCLG for any chemical that causes cancer is zero. Since it might not be possible to restore contaminated groundwater to a pristine condition, MCLGs do not provide meaningful values for practical application to groundwater contaminated by carcinogens.

EPA-derived Maximum Contaminant Levels (MCLs) are federal standards adopted for the regulation of public drinking water in Minnesota. However, MCLs incorporate a consideration of the costs required to reduce contaminant concentrations of a given level and the technological feasibility of reaching that level. The factors that determine economic and technological feasibility for public drinking water systems may not be relevant to private drinking water wells or to other sites impacted by contamination.

EPA-derived Drinking Water Equivalent Levels (DWELs) and Health Advisories (HAs) are estimates of acceptable drinking water levels of noncarcinogens based on health effects information. DWELs and HAs serve as technical guidance to assist federal, state, and local officials. DWELs assume that all of an individual's exposure to a contaminant is from drinking water. HRLs and lifetime HAs take into account people's exposure via routes other than drinking water, and allocate to drinking water only a portion of an individual's allowable exposure (i.e., incorporate the RSC). HAs may also be derived for exposure durations of one day, ten days, or a lifetime. One-day and ten-day HAs incorporate intake and body weight parameters appropriate for children but do not incorporate an RSC. MCLGs, MCLs, DWELs, and lifetime HAs are calculated for adult intake and body weight.

B. PERFORMANCE-BASED RULES

The proposed amendments allow risk managers and stakeholders flexibility in determining how best to protect the public from potentially harmful substances in our groundwater. HRLs provide a scientific and policy context within which the risks posed by a particular situation may be analyzed. After the analysis of risk, risk managers and stakeholders, which may include other regulatory agencies, may examine options, make decisions about which options to implement, take action, and evaluate outcomes.

C. ADDITIONAL NOTICE

MDH followed (and intends to follow) the requirements specified by the Minnesota APA (*Minnesota Statutes*, sections 14.001 *et seq*.) for the publication of official notices in the *State Register* and related procedures, as described below.

- Request for Comments: MDH published the *Request for Comments* notice in the *State Register* (Vol. 34, No. 38, page 1,263) on March 22, 2010. The notice

described the nature of the possible amendments to the current HRL rules and invited public comments. MDH received no comments in response to the publication. On March 30, 2010, MDH also mailed a copy of this notice to the parties listed on MDH's rulemaking list (per *Minnesota Statutes,* section 14.14, subdivision 1a). More than 60 days have elapsed since its publication.

- Notice of Intent to Adopt: MDH intends to publish the *Notice of Intent to Adopt – Dual Notice* in the *State Register*. MDH will mail the proposed rules and the *Notice of Intent to Adopt* to the parties listed on MDH's rulemaking list under *Minnesota Statutes*, section 14.14, subdivision 1a. MDH will also send the *Notice of Intent to Adopt – Dual Notice* and a copy of the SONAR to the Legislature and the Legislative Reference Library. Copies of the proposed rules and the SONAR will be made available at no charge, upon request.

MDH's Notice Plan did not include notifying the Commissioner of Agriculture or the state Council on Affairs of Chicano/Latino People because the rules do not affect farming operations per *Minnesota statutes*, section 14.111, or the Chicano/Latino people per *Minnesota statutes*, section 3.922.

In addition to the APA requirements, MDH also engaged in outreach efforts to inform stakeholders and the public about the 2010 HRL rule amendments. MDH hosted a public meeting and routinely posted updates on its web pages, sent electronic announcements through its e-mail subscription list and published articles about the amendments in newsletters of other local organizations. Details of MDH's outreach efforts are described below.

- MDH HRL rule amendment website: MDH created new web pages on the 2010 HRL rule amendment.[5] The web pages are periodically updated and include information such as: drafts of the proposed amendments to the rules (made available online prior to MDH's HRL public meeting-see details below), the SONAR, notices requesting public input/comments, public meeting announcement and related handouts, the rule amendment schedule, explanations of the rulemaking process, and profiles of technical staff.

- MDH e-mail subscription service: MDH maintains an e-mail subscription list to send updates on groundwater rules and guidance on the chemicals reviewed. MDH routinely sends updates on the HRL rule amendment to the e-mail subscribers. The updates include information such as: the publication of notices requesting comments, announcements regarding the public meeting, and the

[5] MDH's amendments to the rules on Health Risk Limits for Groundwater are available at: http://www.health.state.mn.us/divs/eh/risk/rules/water/amendment.html

availability of drafts of the proposed rules and the SONAR. As of July 26, 2010, MDH's e-mail subscription service has 1,123 subscribers.

- MDH HRL rule amendment public meeting: MDH hosted a public meeting on May 19, 2010. At this meeting, MDH staff gave an overview of the chemical selection and review process, and presented information on the proposed amendments and the types of guidance MDH develops for groundwater contaminants. MDH encouraged attendees to ask questions, engage in discussion with staff and submit written comments. MDH offered to meet with stakeholders upon request but did not receive any follow-up comments or requests for meetings. All of the meeting materials, including answers to the questions asked at the meeting were made available on MDH's HRL rule amendments web pages following the public meeting.[6] Including MDH staff, 20 persons attended the public meeting.

- Other: MDH provided advance notice to key stakeholders from industry, non-profit and partner government agencies of its intent to amend the existing HRL rules. MDH provided information on the scope of the amendments and related MDH projects, and offered to answer technical or rulemaking-related questions/concerns. The calls were made during the first two weeks of March 2010. MDH received no questions or requests for meetings in response.

  In addition, MDH also e-mailed persons who attended the 2009 HRL rules hearing about the intent to amend the existing HRL rules in 2010. The email described the nature and scope of the amendments and the date of publication of the *Request for Comments* in the *State Register*. The e-mails were sent on March 19, 2010.

  MDH also included announcements and articles on the HRL rule amendment on the websites and electronic newsletters of local organizations such as the Freshwater Society, the Minnesota Environmental Partnership (MEP), and the Minnesota Groundwater Associations (MGWA).

[6] Materials and handouts for MDH's meeting on the amendments to the rules on Health Risk Limits for Groundwater are available at:
http://www.health.state.mn.us/divs/eh/risk/rules/water/publicinput.html#stakeholder

D. IMPACT OF PROPOSED RULES

1. CONSULTATION WITH MMB ON LOCAL GOVERNMENT IMPACT

As required by *Minnesota Statutes*, section 14.131, MDH consulted with the Minnesota Management and Budget (MMB) on the impact the proposed rules might have on local governments. MDH did so by sending to the MMB Commissioner, copies of the documents sent to the Governor's Office for review and approval before MDH published the *Notice of Intent to Adopt*. The documents sent to MMB included: the Governor's Office Proposed Rule and SONAR Form; the proposed rules; and the SONAR. MDH sent these documents to MMB on August 10, 2010.

2. DETERMINATION ABOUT RULES REQUIRING LOCAL IMPLEMENTATION

As required by *Minnesota Statutes*, section 14.128, subdivision 1, MDH has considered whether the proposed rules will require a local government to adopt or amend any ordinance or other regulation in order to comply with these rules. MDH has determined that they *do not* because no local government develops or enforces (through ordinances or regulations) groundwater quality standards. Local government has consulted with MDH on the use of HRL values for interpreting the results of well monitoring.

3. COST OF COMPLYING FOR SMALL BUSINESS OR CITY

MDH *cannot* determine small business or city costs incurred in complying with the proposed amendments because the rules do not have any implementation, regulation or enforcement requirements. The amendments simply provide health-based guidance for groundwater contaminants; the rules do not address any application or use. The guidance is one set of criteria for risk managers to evaluate potential health risks from contaminated groundwater. Risk managers have the flexibility in determining if and when to apply the HRL values and how costs should be considered. MDH is unaware of any small business or city that applies the health-based guidance.

E. List of Witnesses

MDH intends to publish the *Notice of Intent to Adopt—Dual Notice* and may cancel the scheduled hearing unless 25 or more persons request a hearing. If the proposed rules require a public hearing, MDH anticipates having the following personnel testify in support of the need and reasonableness of the rules:

- Helen Goeden, Risk Assessor, Health Risk Assessment Unit, MDH
- Paul Moyer, Risk Assessor, Health Risk Assessment Unit, MDH
- Kathryn Sande, Risk Assessor, Health Risk Assessment Unit, MDH

V. CONCLUSION

Groundwater is a primary source of drinking water for Minnesotans. The actual or potential use of this resource for drinking purposes is the "highest priority use" of groundwater and is afforded maximum protection by the state (*Minnesota Statutes*, 115.063). The proposed amendments update MDH's human health-based guidance requested and needed by risk managers to protect groundwater and public health. This effort is part of MDH's long-term plan to continue to review, develop, update and add to the HRL rules on groundwater contaminants.

With the proposed amendments, MDH meets its statutory requirements to use methods that are scientific, based on current EPA risk assessment guidelines and provide protections to vulnerable populations (*Minnesota Statutes*, section 103H.201 and *Minnesota Statutes*, section 144.0751). MDH used reasonable and well-established methods promulgated in 2009 (*Minnesota Rules*, part 4717.7830, subp. 2), peer-reviewed data and scientific research in developing the HRL values for each chemical. The proposed amendments align with MDH's mission to protect, maintain and improve the health of all Minnesotans.

APPENDIX A: GLOSSARY OF TERMS USED IN RISK ASSSESSMENT

Acute duration: A period of 24 hours or less.

Additional Lifetime cancer Risk (ALR): The probability that daily exposure to a carcinogen over a lifetime may induce cancer. The Department of Health uses an additional cancer risk of 1×10^{-5} (1 in 100,000) to derive cancer HRLs. One common interpretation of this additional cancer risk is that if a population of 100,000 were exposed, over an extended period of time, to a concentration of a carcinogen at the level of the HRL, at most, one case of cancer would be expected to result from this exposure. Because conservative techniques are used to develop these numbers, they are upper bound risks; the true risk may be as low as zero.

Additivity Endpoint: See *Health risk index endpoint(s).*

Adverse Effect: A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism or reduces an organism's ability to respond to an additional environmental challenge.

$AF_{lifetime}$ or lifetime adjustment factor: An adjustment factor used to adjust the adult-based cancer slope factor for lifetime exposure based on chemical-specific data.

Age-Dependent Adjustment Factor (ADAF): A default adjustment to the cancer slope factor that recognizes the increased susceptibility to cancer from early-life exposures to linear carcinogens in the absence of chemical-specific data. For the default derivation of cancer HRLs the following ADAFs and corresponding age groups are used: $ADAF_{<2}$ = 10, for birth until 2 years of age; $ADAF_{2<16}$ = 3, for 2 up to 16 years of age; and $ADAF_{16+}$ = 1, for 16 years of age and older.

Animal Study: A controlled experiment in which a cohort of test animals, usually mice, rats, or dogs, is exposed to a range of doses of a chemical and assessed for health effects. For the purposes of the MDH HRL rules, only studies of mammalian species were considered; studies relating to fish, amphibians, plants, etc. were not used because of the greater uncertainty involved in extrapolating data for these species to human health effects, as compared to studies involving mammals.

Benchmark Dose (BMD): Dose or concentration that produces a predetermined change in the response rate of an adverse or biologically meaningful effect. The BMD approach uses mathematical models to statistically determine a dose associated with a predefined effect level (e.g., 10 percent).

BMDL: A statistical lower confidence limit on the benchmark dose (BMD).
Biologically Based Dose-Response (BBDR) Model: A predictive model that describes biological processes at the cellular and molecular level linking the target organ dose to the adverse effect.

Cancer classification: Most substances are classified under the system put in place in the U.S. EPA Risk Assessment Guidelines of 1986. This system uses the categories:

- A known human carcinogen;
- B probable human carcinogen;
- C possible human carcinogen;
- D not classifiable as to carcinogenicity; and
- E evidence of non-carcinogenicity for humans.

In 2005, EPA has finalized revised guidelines calling for a "weight of the evidence" narrative, which is a short summary that explains the potential of a substance to cause cancer in humans and the conditions that characterize its expression. The following general descriptors were suggested:

- carcinogenic to humans;
- likely to be carcinogenic to humans;
- suggestive evidence of carcinogenic potential;
- inadequate information to assess carcinogenic potential; and
- not likely to be carcinogenic to humans.

Cancer Slope Factor: See *Slope Factor.*

Carcinogen: Generically, a carcinogen is a chemical agent that causes cancer. For the purposes of these Rules, a carcinogen is a chemical that is:
A) classified as a human carcinogen (Group A) or a probable human carcinogen (Group B) according to the EPA (1986a) classification system. This system has been replaced by a newer classification scheme (EPA 2005), but many chemicals still have classifications under the 1986 system. Possible human carcinogens (Group C) will be considered carcinogens under these Rules if a cancer slope factor has been published by EPA and that slope factor is supported by the weight of the evidence.

OR,

B) Classified pursuant to the Final Guidelines for Carcinogenic Risk Assessment (EPA 2005b) as "Carcinogenic to Humans" or "Likely to be carcinogenic to humans."

See also: *Linear carcinogen, Nonlinear carcinogen.*

CAS number: The Chemical Abstract Service (CAS) Registry Number. This number, assigned by the Chemical Abstracts Service, a division of the American Chemical Society, uniquely identifies each chemical.

Chronic duration: A period of more than approximately 10% of the life span in humans (more than approximately 90 days to 2 years in typically used mammalian laboratory animal species).

Co-critical effect(s): Generally, effects that are observed at doses up to or similar to the exposure level of the critical study associated with the critical effect(s).

Conversion Factor (CF): A factor (1,000 μg/mg) used to convert milligrams (mg) to micrograms (μg). There are 1,000 micrograms per milligram.

Critical effect(s): The health effect or health effects from which a non-cancer toxicity value is derived; usually the first adverse effect that occurs to the most sensitive population as the dose increases.

Database Factor: see Uncertainty Factor.

Developmental health endpoint: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) function deficiency.

Dose-Response Assessment: The determination of the relationship between the magnitude of administered, applied, or internal dose and a specific biological response. Response can be expressed as measured or observed incidence, percent response in groups of subjects (or populations), or the probability of occurrence of a response in a population.

Dosimetric Adjustment Factor (DAF): A multiplicative factor used to adjust observed experimental or epidemiological data to human equivalent concentration for assumed ambient scenario.

Duration: Duration refers to the length of the exposure period under consideration. The default durations evaluated for non-cancer health effects are acute, short-term, subchronic, and chronic. See individual definitions for more information. These definitions are from "A Review of the Reference Dose and Reference Concentration Processes," United States Environmental Protection Agency, Risk Assessment Forum (December 2002, http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55365).

The default durations evaluated for cancer health effects correspond to the age groups upon which the age dependent adjustment factors (ADAF) are based. These age groups were identified in the "Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens," United States Environmental Protection Agency, Risk Assessment Forum (March 2005, http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=160003). The age groups are: from birth up to 2 years of age; from 2 up to 16 years of age; and 16 years of age and older.

The duration of concern may also be determined by chemical-specific information. For example, the non-cancer health effect may be linked to the time point at which the concentration of the chemical in the blood reaches a level associated with an adverse effect. Another example is if the cancer slope factor is based on a lifetime rather than an adult-only exposure protocol. In this case, a lifetime duration rather than the three age groups identified above would be used.

Endocrine (hormone) system: All the organs, glands, or collections of specialized cells that secrete substances (hormones) that exert regulatory effects on distant tissues and organs through interaction with receptors, as well as the tissues or organs on which these substances exert their effects. The hypothalamus, pituitary, thyroid, parathyroids, adrenal glands, gonads, pancreas, paraganglia, and pineal body are all endocrine organs; the intestines and the lung also secrete hormone-like substances.

Endocrine (E): For the purpose of the HRL revision, "endocrine" or "E" means a change in the circulating hormones or interactions with hormone receptors, regardless of the organ or organ system affected. Because of the many organs and tissues that secrete and/or are affected by hormones, the Department has not considered the endocrine system to be a discrete classification of toxicity. An endpoint is given an "E" designation only if a change in circulating hormones or receptor interactions has been measured. Endpoints with or without the (E) designation are deemed equivalent (e.g., thyroid (E) = thyroid) and shall be included in the same Health Risk Index calculation.

Exposure Assessment: An identification and evaluation of the human population exposed to a toxic agent that describes its composition and size and the type, magnitude, frequency, route, and duration of exposure.

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans.

Health-Based Value (HBV): A health-based value (HBV) is the concentration of a groundwater contaminant that can be consumed daily with little or no risk to health. HBVs are derived using the same algorithm as HRLs but have not yet been promulgated as rules. An HBV is expressed as a concentration in micrograms per liter (µg/L).

Health risk index: A health risk index is a sum of the quotients calculated by identifying all chemicals that share a common health endpoint and dividing the measured or surrogate concentration of each chemical by its HRL. The multiple-chemical health risk index is compared to the cumulative health risk limit of 1 to determine whether an exceedance has occurred.

Health risk index endpoint(s): The general description of critical and co-critical effects used to group chemicals for the purpose of evaluating risks from multiple chemicals. For example, the effect "inhibition of acetyl cholinesterase" is listed as the health risk index endpoint "nervous system," and all chemicals that can affect the nervous system would be considered together.

Health Risk Limit (HRL): A health risk limit (HRL) is the concentration of a groundwater contaminant, or a mixture of contaminants that can be consumed with little or no risk to health, and which has been promulgated under rule. A HRL is expressed as a concentration in micrograms per liter (µg/L).

Health Standards Statute: *Minnesota Statutes,* section 144.0751. This statute requires that drinking water and air quality standards include a reasonable margin of safety to protect infants, children, and adults, taking into consideration the risk of a number of specified health effects, including: "reproductive development and function, respiratory function, immunologic suppression or hypersensitization, development of the brain and nervous system, endocrine (hormonal) function, cancer, and general infant and child development."

Human Equivalent Concentration (HEC): The human concentration (for inhalation exposure) of an agent that is believed to induce the same magnitude of toxic effect as the experimental animal species concentration. This adjustment may incorporate toxicokinetic information on the particular agent, if available, or use a default procedure.

Human Equivalent Dose (HED): The human dose (for other than the inhalation routes of exposure) of an agent that is believed to induce the same magnitude of toxic effect as the experimental animal species dose. This adjustment may incorporate toxicokinetic information on the particular agent, if available, or use a default procedure, such as assuming that daily oral doses experienced for a lifetime are proportional to body weight raised to the 0.75 power ($BW^{3/4}$).

Immunotoxicity: Adverse effects resulting from suppression or stimulation of the body's immune response to a potentially harmful foreign organism or substance. Changes in immune function resulting from immunotoxic agents may include higher rates or more severe cases of disease, increased cancer rates, and auto-immune disease or allergic reactions.

Immune system: A complex system of organs, tissues, cells, and cell products that function to distinguish self from non-self and to defend the body against organisms or substances foreign to the body, including altered cells of the body, and prevent them from harming the body.

Intake Rate (IR): Rate of inhalation, ingestion, and dermal contact, depending on the route of exposure. For ingestion of water, the intake rate is simply the amount of water, on a per body weight basis, ingested on a daily basis (liters per kg body weight per day, L/kg-day) for a specified duration. For the derivation of non-cancer and cancer HRLs, the time-weighted average of the 95th percentile intake rate for the relevant duration was used.

Interspecies Factor: see *Uncertainty Factor.*

Intraspecies Factor: see *Uncertainty Factor.*

Kilogram (kg): One kilogram is equivalent to 2.2046226 pounds.

Latency Period: The time between exposure to an agent and manifestation or detection of a health effect of interest.

Linear carcinogen: A chemical agent for which the associated cancer risk varies in direct proportion to the extent of exposure, and for which there is no risk-free level of exposure.

Linear Dose Response: A pattern of frequency or severity of biological response that varies directly with the amount of dose of an agent. This linear relationship holds only at low doses in the range of extrapolation.

Liter (L): One liter is equivalent to 1.05671 quarts.

Liters per kilogram per day (L/kg-day): A measure of daily water intake, relative to the individual's body weight.

LOAEL-to-NOAEL: see *Uncertainty Factor.*

Lowest Observed Adverse Effect Level (LOAEL): The lowest exposure level at which a statistically or biologically significant increase in the frequency or severity of adverse effects is observed between the exposed population and its appropriate control group. A LOAEL is expressed as a dose rate in milligrams per kilogram body weight per day (mg/kg-day).

MCL-based HRL: A Health Risk Limit for groundwater adopted by reference to the U.S. EPA's Maximum Contaminant Level (MCL) rather than through the standard MDH chemical evaluation process.

Mechanism of Action: The complete sequence of biological events (i.e., including toxicokinetic and toxicodynamic events) from exposure to the chemical to the ultimate cellular and molecular consequences of chemical exposure that are required in order to produce the toxic effect. However, events that are coincident but not required to produce the toxic outcome are not included.

Microgram (μg): 10^{-6} grams or 10^{-3} milligrams. 1,000 micrograms = 1 milligram

Micrograms per liter (μg/L): A unit of measure of concentration of a dissolved substance in water.

Milligram (mg): 10^{-3} grams. 1,000 milligrams = 1 gram.

Milligrams per kilogram of body weight per day (mg/kg-day): A measure of daily exposure to a contaminant, relative to the individual's body weight.

Mode of Action (MOA): The sequence of key event(s) (i.e., toxicokinetics and toxicodynamics) after chemical exposure upon which the toxic outcomes depend.

Neurotoxicity: Neurotoxicity is any adverse effect on the structure or function of the central and/or peripheral nervous system related to exposure to a chemical.

Nonlinear carcinogen: A chemical agent for which, particularly at low doses, the associated cancer risk does not rise in direct proportion to the extent of exposure, and for which there may be a threshold level of exposure below which there is no cancer risk.

Nonlinear Dose Response: A pattern of frequency or severity of biological response that does not vary directly with the amount of dose of an agent. When mode of action information indicates that responses may fall more rapidly than dose below the range of the observed data, nonlinear methods for determining risk at low dose may be justified.

No observed adverse effect level (NOAEL): An exposure level at which there is no statistically or biologically significant increase in the frequency or severity of adverse effects between the exposed population and its appropriate control group.

Physiologically Based Toxicokinetic (PBTK) Model: A model that estimates the dose to a target tissue or organ by taking into account the rate of absorption into the body, distribution among target organs and tissues, metabolism, and excretion. (Also referred to as physiologically based pharmacokinetic model.)

Point of Departure (POD): The dose-response point that marks the beginning of a low-dose extrapolation. This point can be the lower bound on dose for an estimated incidence or a change in response level from a dose-response model (BMD) or a NOAEL or LOAEL for an observed incidence, or change in level of response.

Precursor Event: An early condition or state preceding the pathological onset of a disease.

Reference Dose (RfD): An estimate of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects for a given exposure duration. It is derived from a suitable exposure level at which there are few or no statistically or biologically significant increases in the frequency or severity of an adverse effect between an exposed population and its appropriate control group. The RfD is expressed in units of milligrams of the chemical per kilogram of body weight per day (mg/kg-day).

Relative Source Contribution (RSC): The percentage (or fraction) of an individual's total permissible exposure to a substance or chemical that is "allocated" to ingestion of water. Application of this factor acknowledges that non-ingestion exposure pathways (e.g., dermal contact with water, inhalation of volatilized chemicals in water) as well as exposure to other media, such as air, food, and soil may occur. The *Minnesota Groundwater Protection Act*, in *Minnesota Statutes*, section 103H.201, subd. (1)(d), requires that MDH use a relative source contribution in deriving health risk limits for systemic toxicants. MDH relied upon EPA's Exposure Decision Tree approach (http://www.epa.gov/waterscience/criteria/humanhealth/method/method.html) to determine appropriate RSC values.

HRLs are often applied at contaminated sites where media other than groundwater may also be contaminated. The level of media contamination and the populations potentially exposed will vary from site to site and from chemical to chemical. Using a qualitative evaluation and the Exposure Decision Tree, MDH determined the following default RSC values: 0.2 for highly volatile contaminants (chemicals with a Henry's Law Constant greater than 1×10^{-3} atm-m^3/mole) and 0.5 for young infants or 0.2 for older infants, children and adults for chemicals that are not highly volatile. There may be site-specific situations where the Exposure Decision Tree along with site-specific information could be used to derive a site-specific RSC.

Reproductive toxicity: For the purpose of the HRL revision, effects on the ability of males or females to reproduce, including effects on endocrine systems involved in reproduction and effects on parents that may affect pregnancy outcomes. Reproductive toxicity may be expressed as alterations in sexual behavior, decreases in fertility, changes in sexual function that do not affect fertility, or fetal loss during pregnancy.

Risk: In the context of human health, the probability of adverse effects resulting from exposure to an environmental agent or mixture of agents.

Risk Assessment: The evaluation of scientific information on the hazardous properties of environmental agents (hazard characterization), the dose-response relationship (dose-response assessment), and the extent of human exposure to those agents (exposure assessment). The product of the risk assessment is a statement regarding the probability that populations or individuals so exposed will be harmed and to what degree (risk characterization).

RAA: Risk Assessment Advice
A type of MDH health-based guidance that evaluates potential health risks to humans from exposures to a chemical. Generally, RAA contains greater uncertainty than HRLs and HBVs due to limited availability of information. Based on the information available, RAA may be quantitative (e.g., a concentration of a chemical that is likely to pose little or no health risk to humans expressed in μg/L) or qualitative (e.g., a written description of how toxic a chemical is in comparison to a similar chemical).

Risk Characterization: The integration of information on hazard, exposure, and dose-response to provide an estimate of the likelihood that any of the identified adverse effects will occur in exposed people.

Risk Management: A decision-making process that accounts for political, social, economic, and engineering implications together with risk-related information in order to develop, analyze, and compare management options and select the appropriate managerial response to a potential health hazard.

Secondary Effect(s): Generally a health effect or health effects observed in any of a number of studies that occurred within three-fold of the exposure level in the critical study associated with the critical effect(s).

Secondary Observation: Notation indicating that although endpoint-specific testing was not conducted, observations regarding effects on the endpoint were reported in a toxicity study.

Short-Term Duration: A period of more than 24 hours, up to 30 days.

Slope Factor (SF): An upper-bound estimate of cancer risk per increment of dose that can be used to estimate risk probabilities for different exposure levels. This estimate is generally used only in the low-dose region of the dose-response relationship; that is, for exposures corresponding to risks less than 1 in 100. A slope factor is usually expressed in units of cancer incidence per milligram of chemical per kilogram of body weight per day (per [mg/kg-day] or $[mg/kg\text{-}day]^{-1}$).

Statistical Significance: The probability that a result is not likely to be due to chance alone. By convention, a difference between two groups is usually considered statistically significant if chance could explain it only 5% of the time or less. Study design considerations may influence the a priori choice of a different level of statistical significance.

Subchronic Duration: A period of more than 30 days, up to approximately 10% of the life span in humans (more than 30 days up to approximately 90 days in typically used mammalian laboratory animal species).

Subchronic-to-Chronic Factor: See *Uncertainty Factor*.

Target Organ: The biological organ(s) most adversely affected by exposure to a chemical or physical agent.

Time-Weighted Average (TWA): In quantifying a measurement that varies over time, such as water intake, a time-weighted average takes measured intakes, which may occur at unevenly-spaced intervals, and multiplies each measurement by the length of its interval. These individual weighted values are then summed and divided by the total length of *all* of the individual intervals. The result is an average of all of the measurements, with each measurement carrying more or less weight in proportion to its size.

Threshold: The dose or exposure below which no deleterious effect is expected to occur.

Toxicity: Deleterious or adverse biological effects elicited by a chemical, physical, or biological agent.

Toxicodynamics (TD): The determination and quantification of the sequence of events at the cellular and molecular levels leading to a toxic response to an environmental agent (sometimes referred to as pharmacodynamics and also MOA).

Toxicokinetics (TK): The determination and quantification of the time course of absorption, distribution, metabolism, and excretion of chemicals (sometimes referred to as pharmacokinetics).

Uncertainty Factor (UF): One of several factors used in deriving a reference dose from experimental data. UFs are intended to account for:

- **Interspecies UF** - the uncertainty in extrapolating from mammalian laboratory animal data to humans (denoted as 3A or 10A);
- **Intraspecies Variability Factor** - the variation in sensitivity among the members of the human population (denoted as 3H or 10H);

- **Subchronic-to-Chronic Factor** (Use of a less-than-chronic study for a chronic duration) - the uncertainty in extrapolating from effects observed in a shorter duration study to potential effects from a longer exposure (denoted as $3_{S\text{-}to\text{-}C}$ or $10_{S\text{-}to\text{-}C}$);
- **LOAEL-to-NOAEL** (Use of a LOAEL rather than a NOAEL) - the uncertainty associated with using a study in which health effects were found at all doses tested (denoted as $3_{L\text{-}to\text{-}N}$ or $10_{L\text{-}to\text{-}N}$); and
- **Database Uncertainty** - the uncertainty associated with deficiencies in available data (denoted as 3DB or 10DB).

Uncertainty factors are normally expressed as full or half powers of ten, such as 10^0 (=1), $10^{0.5}$ (≈3), and 10^1 (=10). All applicable uncertainty factors are multiplied together to yield a composite uncertainty factor for the RfD. Half-power values such as $10^{0.5}$ are factored as whole numbers when they occur singly but as powers or logs when they occur in tandem (EPA 2002c). Therefore, a composite UF using values of 3 and 10 would be expressed as 30 (3×10^1), whereas a composite UF using values of 3 and 3 would be expressed as 10 ($10^{0.5} \times 10^{0.5} = 10^1$).

Uncertainty and variability factors are typically values of three or ten and are multiplied together. The Department has not developed a HRL if the product of all uncertainty factors exceeds 3,000.

Volatile: Volatility is the tendency of a substance to evaporate. Inhalation exposure to volatile chemicals in groundwater may be a health concern. Chemical characteristics that affect volatility include molecular weight, polarity, and water solubility. Typically, a chemical is considered volatile if it has a Henry's law constant greater than 3×10^{-7} atm-m^3/mol. Chemicals are characterized as being nonvolatile, or being of low, medium, or high volatility as follows:

- Henry's Law constant < 3×10^{-7} atm-m^3/mol = nonvolatile
- Henry's Law constant > 3×10^{-7} to 1×10^{-5} atm-m^3/mol = low volatility
- Henry's Law constant >1×10^{-5} to 1×10^{-3} atm-m^3/mol = moderate volatility
- Henry's Law constant >1×10^{-3} atm-m^3/mol = high volatility

Weight of Evidence (WOE): An approach requiring a critical evaluation of the entire body of available data for consistency and biological plausibility. Potentially relevant studies should be judged for quality and studies of high quality given much more weight than those of lower quality.

APPENDIX B: BIBLIOGRAPHY

Note: The following references were used to develop an updated methodology and Health Risk Limit values in MDH's effort on revising and updating the rules on Health Risk Limits for Groundwater. These materials are available for review online, or at the Minnesota Department of Health, or through the Minitex Interlibrary Loan System.

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APPENDIX C: CONCEPTS USED IN MDH-DERIVED HRLs

Described below are the basic principles that underlie MDH's risk algorithm promulgated in 2009 (*Minnesota Rules,* part 4717.7830, subp. 2) as stated in Section I.D. MDH used these methods to derive the HRL values that are included in the 2010 proposed amendments. Detailed descriptions of these concepts are also available in MDH's 2008 SONAR (MDH, 2008. See Part IV).[2]

HRL rules employ two types of assessments. One assessment is for chemicals for which it is assumed that any dose of that chemical above zero carries some potential increased risk of cancer. These chemicals are identified as "linear" or "non-threshold" carcinogens. None of the chemicals included in these rule amendments are linear carcinogens. The second type of assessment is for evaluating non-cancer effects. This method can also be applied to address chemicals that have the potential to cause cancer through a "nonlinear" mechanism. The assessment of a noncarcinogen or a nonlinear carcinogen assumes that there is a threshold dose that must be exceeded before adverse health effects (including cancer) will develop.

1. TOXICITY

Toxicity is one of the factors in determining HRLs. In evaluating the dose and response, researchers seek to determine the lowest dose at which adverse effects are observed (the "lowest observed adverse effect level," or LOAEL) and the highest dose at which no adverse effects are observed (the "no observed adverse effect level," or NOAEL). Alternatively, researchers may statistically model the data to determine the dose expected to result in a response in a small percentage of the dosed animals (e.g., the benchmark dose, or BMD). The dose resulting from the dose-response evaluation also referred to as a point-of-departure (POD) dose serves as the starting point for deriving health-protective concentrations for air, water and soil, collectively referred to as the "environmental media."

For effects other than cancer, the dose selected from the dose-response evaluation is divided by variability and uncertainty factors (UFs) to account for what is not known about a chemical's toxicity to a human population. The result, called a reference dose (RfD), is an estimate of a dose level that is likely to be without an appreciable risk of adverse effects. An RfD is expressed in milligrams of chemical per kilogram of body weight per day (mg/kg-day).

Understanding the relationship between the timing and duration of exposure and the subsequent adverse effect is essential in deriving criteria that are protective of sensitive life stages (e.g., development early in life) and short periods of high exposure (e.g., infancy). In *A Review of the Reference Dose (RfD) and Reference Concentration (RfC) Processes,* EPA recommends the derivation of acute, short-term, subchronic, and chronic

RfDs (EPA 2002c). In cases where sufficient toxicological information is available, MDH derives RfDs for the various time periods as defined by EPA.

In evaluating the 2010 proposed HRLs, MDH staff compiled and assessed the available toxicity information for the following durations of exposure:

- Acute: up to 24 hours
- Short-term: greater than 24 hours and up to 30 days
- Subchronic: greater than 30 days and up to 10% of a lifetime
- Chronic: greater than 10% of a lifetime.

The current HRL methods not only list the specific effects occurring at the lowest effect dose, but also effects that occur at doses similar to the Lowest-Observed-Adverse Effect Level (LOAEL), perhaps from other available toxicity studies. This provides more information to risk managers and can affect the results of an assessment when multiple chemicals are present (also see *Minnesota Rules*, part 4717.7880). MDH has also indicated which chemicals are associated with endocrine effects and which chemicals have their greatest effects as a result of exposure *in utero* or during child development. In the chemical summary sheets (see Appendix E) that include the derivation of HRL values, MDH notes whether the information reviewed for each chemical includes assessments of developmental, reproductive, immunological, endocrine, or neurological effects. This information is provided for each chemical in part to meet the stipulations of the *2001 Health Standards Statute*.

The sources of toxicity information that MDH considered in deriving HRLs include the following:

- U.S. Environmental Protection Agency (EPA)
    - Reregistration Eligibility Decisions (REDs) from the Office of Pesticide Programs
    - The Health Effects Support Documents for Contaminant Candidate List Regulatory Determination from the Office of Ground Water and Drinking Water
    - The Integrated Risk Information System (IRIS)
    - The National Center for Environmental Assessment (NCEA) risk assessments
- California EPA
    - The Public Health Goal technical support documents from the Office of Environmental Health Hazard Assessment (OEHHA)
- Agency for Toxic Substances and Disease Registry (ATSDR) toxicological profiles;
- National Toxicology Program (NTP) study report and toxicity studies;
- Health Canada's Priority Substances Assessment Program and Screening Assessment Reports
- European Commission chemical reviews

    - European Commission Enterprise and Industry Chemicals
    - European Food Safety Authority
    - European Union Pesticide Database
- The World Health Organization's (WHO) Concise International Chemical Assessment Documents; and
- Other published scientific literature.

2. Intake Rates

An intake rate (IR) is defined as the rate of ingestion of water (*Minnesota Rules*, part 4717.7820, subp. 14). In deriving HRLs, the RfD for non-cancer health effects is converted from milligrams per kilogram body weight per day (mg/kg-day) to a water concentration in micrograms per liter of water (µg/L) by dividing by a water intake rate. IR is expressed as the quantity of water consumed in liters per kilogram of body weight per day (L/kg-day).

MDH staff calculated and used the following default time-weighted-average intake rates:

- Acute: 0.289 L/kg-day
- Short-term: 0.289 L/kg-day
- Subchronic: 0.077 L/kg-day
- Chronic: 0.043 L/kg-day

These default values are time-weighted averages based on the data reported in EPA's Per Capita Report (EPA 2004c) and a revised assessment for the Child-Specific Exposure Factors Handbook (EPA, 2007b).

MDH staff considered whether chemical specific intake rates were more appropriate to use than the default intake rates. The default intake rates were used for all of the 2010 proposed HRL chemicals with the following exceptions:

- The short-term HRL for perfluorobutane sulfonate (PFBS) uses a chemical specific intake rate of 0.245 L/kg-day based on a four month exposure rather than the default short-term value.
- The acute and short-term HRLs for ethylene glycol use the pregnant woman intake rate of 0.043 L/kg-day rather than the default acute and short-term values.

For more specific information for assessments of PFBS and ethylene glycol, see the chemical-specific summary sheets in Appendix E.

The relative source contribution (RSC) was used to allocate a portion of the total daily RfD to exposure from ingestion of water. The balance of the RfD is reserved for other exposures, such as exposures from non-ingestion routes of exposure to water (e.g., inhalation of volatilized chemicals, dermal absorption) as well as exposures via other contaminated media such as food, air, and soil. *Minnesota Statutes*, section 103H.201, subd. (1)(c) which establishes methods for deriving HRLs for chemicals other than linear

(non-threshold) carcinogens requires that an RSC be used. The RSC values used are based on the EPA Ambient Water Quality Criteria document (EPA 2000c) and the consideration of chemical and physical properties of each chemical (e.g. volatility).

Based on qualitative evaluation and the EPA's Exposure Decision Tree (EPA 2000c), MDH used the following default RSC values: for non-volatile, low and moderately volatile chemicals, an RSC of 50 percent (0.5) is used for the acute and short-term durations that utilize the intake rate for young infants or 20 percent (0.2) for subchronic and chronic durations. In contrast, the RSC of 20 percent (0.2) is used for all durations for highly volatile chemicals because inhalation exposure would be a concern for any duration or age of exposure, including infancy. The volatility classification for each chemical is determined by the following definition (*Minnesota Rules*, part 4717.7820, subp. 25):

- Nonvolatile – Henry's Law constant <3 × 10-7 atm-m3/mol
- Low volatility – Henry's Law constant >3 × 10-7 to 1 × 10-5 atm-m3/mol
- Moderate volatility – Henry's Law constant >1 × 10-5 to 1 × 10-3 atm-m3/mol
- High volatility – Henry's Law constant > 1 × 10-3 atm-m3/mol

3. UNCERTAINTY FACTORS (UFS)

To account for what is not known about a chemical's toxicity to a human population, uncertainty and variability factors are applied to derive HRLs for non-cancer and nonlinear carcinogens. Once the dose level (e.g., NOAEL, LOAEL or BMD) has been selected as the point of departure (POD), it is then divided by uncertainty and/or variability factors to derive the RfD:

$$\frac{\text{Point of Departure (POD)}}{\text{Uncertainty and Variability Factors (UFs)}} = \text{Reference Dose (RfD)}$$

As risk assessment methods have evolved, risk assessors consider the application of five uncertainty and variability factors. Each of these factors and guidelines for application are explained below:

- Interspecies Extrapolation Factor – This factor accounts for the uncertainty or the difference between animals and humans when laboratory animal data are used as the source of the POD. It is composed of two subfactors – toxicokinetics (absorption, distribution, metabolism and elimination of the chemical) and toxicodynamics (the body's response to the chemical). If there is no information regarding quantitative differences between laboratory animals and humans for either subfactor, a default value of 10 is used. If information is available for one of the two subfactors, then the chemical specific information along with a default factor of 3 (half of 10 on a logarithmic scale equals ~3.16 rounded to 3) is used for the remaining subfactor. NOTE: chemical specific information may lead to a

combined factor of greater than 10. If human data is the source of the POD then a value of 1 may be used.

- Intraspecies Variability Factor – This factor accounts for the variation in sensitivity between individuals in the human populations (including life stages) and for the fact that some subpopulations might be more sensitive to the toxicological effects than the average population. As with the interspecies extrapolation factor, this factor is also composed of two subfactors – toxicokinetics and toxicodynamics. If no information on human variability is available then a default value of 10 is used. If adequate information is available for either subfactor then this information is used along with a default factor of 3 for the remaining subfactor. If the POD is based on human data gathered in the known sensitive subpopulations, a value of less than 10 (including 1) may be chosen.

- Subchronic-to-Chronic Extrapolation Factor – This factor accounts for the uncertainty in extrapolating from the effects observed in a shorter-duration study to potential effects of longer-duration exposure due to lack of adequate information in the dataset. In determining whether to apply this factor, MDH considers: 1) data indicating other, more sensitive, health effects as the duration of exposure increases, 2) data indicating that the critical effect(s) progress in severity as exposure duration increases, or 3) data indicating that the POD decreases in value as exposure duration increases. A default value of 10 is often applied to shorter-duration PODs to derive chronic values unless data suggest a lack of progression with increasing exposure duration. If data addresses only some of the considerations, a value of less than 10 (e.g., 3) may be used.

- LOAEL-to-NOAEL Extrapolation Factor – This factor accounts for the uncertainty in using a study in which even the lowest dose tested causes some adverse effect(s), and is in contrast to the preferred case where at least one of the administered doses caused no adverse effects. Since the RfD is considered to be a threshold value that protects against any adverse health effects, the LOAEL-to-NOAEL factor is applied when the critical study(s) lacks information or the threshold/NOAEL can not be determined with confidence (e.g., when LOAEL is used as a POD). The default value is 10, however, if the adverse effect observed is considered to be of minimal severity a default value of 3 may be appropriate.

- Database Uncertainty Factor – This factor accounts for uncertainty based on existing data or deficiencies in the available dataset, resulting in the potential for additional data to yield a lower reference value (EPA 2004a) (i.e. additional studies may show the chemical to be more harmful). A high-confidence database would contain a minimum of two chronic bioassays testing system toxicity by the appropriate route of exposure in different species, one 2-generation

reproductive toxicity study, and two developmental toxicity studies in different species. A database UF is used when a potentially more sensitive health effect cannot be identified because the database is missing a particular type of study or the existing data suggest the potential for a health effect but the effect has not been adequately assessed. In general, a default factor of 10 is used if more than one particular type of study is missing. A value of 3 has been used if one particular type of study is missing (e.g., no 2-generation reproductive or developmental study).

In the absence of chemical-specific information, each of the five factors is typically assigned a value between 1 and 10. Uncertainty factors are normally expressed as full or half powers of ten, such as 10^0 (=1), $10^{0.5}$ (≈3), and 10^1 (=10). All applicable uncertainty factors are multiplied together to yield a composite uncertainty factor for the RfD. Half-power values such as $10^{0.5}$ are factored as whole numbers when they occur singly but as powers or logs when they occur in tandem (EPA 2002c). Therefore, a composite UF using values of 3 and 10 would be expressed as 30 (3×10^1), whereas a composite UF using values of 3 and 3 would be expressed as 10 ($10^{0.5} \times 10^{0.5} = 10^1$).

In keeping with the EPA RfC/RfD Technical Panel (EPA 2002c) recommendation and the rationale supporting it, MDH has not derived a HRL for any chemical if the product of all applicable uncertainty factors exceeds 3,000 (*Minnesota Rules*, part 4717.7820, subp. 21). Chemicals with higher total uncertainty factors are not necessarily more toxic than chemicals with lower total uncertainty factors. The use of a larger total uncertainty factor only means that there is less information is available about the toxicity of the chemical.

APPENDIX D: SELECTION OF 2010 CONTAMINANTS

Note: The selection of the contaminants/chemicals for the 2010 amendments was based on input from programs within MDH (such as the Site Assessment and Consultation Unit or SAC) as well as partner state agencies such as the Minnesota Pollution Control Agency (MPCA) and the Minnesota Department of Agriculture (MDA). At past interagency meetings (held on August 23, 2007 and May 8, 2008), representatives from these agencies nominated chemicals for review and discussed their concerns and priorities. Noted below are the 2010 chemicals and the inter-agency meetings at which chemicals were nominated for guidance requests.

Table 1: Inter-agency Meetings to Request for Guidance on Groundwater Contaminants

Inter-agency Meeting to Request Guidance	**Chemical**	**Inter-agency Meeting to Request Guidance**	**Chemical**
August-07	Acetochlor ESA	May-08	Metolachlor & s-Metolachlor
May-08	Acetochlor OXA	August-07	Metolachlor ESA
May-08	Acetone	May-08	Metolachlor OXA
August-07	Dichlorodifluoromethane	March-07*	Perfluorobutane sulfonate (PFBS)
August-07	1,1-Dichloroethene (Vinylidene chloride)	August-07	Perfluorobutyrate (PFBA)
August-07	Ethylbenzene	August-07	Toluene
August-07	Ethylene glycol	May-08	Xylenes (Mixture of isomers, o, m, p)

* Guidance requested by MDH's Site Assessment and Consultation (SAC) Unit

APPENDIX E: CHEMICAL SUMMARY SHEETS

Note: The following documents represent the Health Based Values (HBVs) for chemicals included in the 2010 proposed amendments. These chemical summary sheets are also available on MDH's Groundwater Values Table[4] and the HRL rule amendment webpages.[5] Upon adoption of the 2010 amendments, these HBV summary sheets will be updated as HRL summary sheets, and posted online.

2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: July 2009
Expiration Date: July 2014

Chemical Name: Acetochlor ESA
CAS #: 187022-11-3
Synonyms: Acetochlor Ethane Sulfonic Acid; CP92429-2, MON 53754

Acute Non-Cancer Health-Based Value ($nHBV_{acute}$) = Insufficient data

Short-term Non-Cancer HBV ($nHBV_{short\text{-}term}$) = 600 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.37 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 640 rounded to **600 ug/L**

Reference Dose:	0.37 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	370.3 mg/kg-d (minimal LOAEL, MRID 45300503 as cited by EPA 2000a and 2006b)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	1000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 3 minimal LOEL-to-NOAEL, 3 for database insufficiency (lack of multigenerational reproductive or developmental studies)
Critical effect(s):	Dose-related increase in thyroid stimulating hormone (TSH) and free thyroxine (T4)
Co-critical effect(s):	None
Additivity endpoint(s):	Thyroid (E)
Secondary effect(s):	None

Subchronic Non-Cancer HBV ($nHBV_{subchronic}$) = 600 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.23 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 597 rounded to **600 ug/L**

Reference Dose:	0.23 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	225.4 mg/kg-d (NOAEL, MRID 45313801 as cited by EPA 2000 and 2006)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	1000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive or developmental studies; insufficient studies for neurological and endocrine effects; lack of studies in a second species)
Critical effect(s):	Decreased food utilization, adult body weights and body weight gains
Co-critical effect(s):	Alterations in serum thyroid hormone levels
Additivity endpoint(s):	Thyroid (E) (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Chronic Non-Cancer HBV ($nHBV_{chronic}$) = 300 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.075 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 349 rounded to **300 ug/L**

Reference Dose:	0.075 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	225.4 mg/kg-d (NOAEL, MRID 45313801 as cited by

	EPA 2000 and 2006)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	3,000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive or developmental studies; insufficient studies for neurological and endocrine effects; lack of studies in a second species (dogs have been shown to be more sensitive)), and 3 for use of a subchronic study (based on consideration of a comparison of the 28 and 90 day studies, however, this comparison was considered inadequate to completely remove this UF).
Critical effect(s):	Decreased food utilization, adult body weights and body weight gains
Co-critical effect(s):	Alterations in serum thyroid hormone levels
Additivity endpoint(s):	Thyroid (E) (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Cancer HBV (cHBV) = Not Applicable

Cancer classification:	Acetochlor ESA has not been classified as to its carcinogenic potential. However, EPA has indicated that it is unlikely to be carcinogenic (EPA 2004, EPA 2006b). The parent, acetochlor, is classified as "likely" to be carcinogenic and is considered to be a nonlinear carcinogen (i.e., there is a threshold level of exposure below which there is no cancer risk).

Volatile: No

Summary of Guidance Value History:
There is no 1993/94 HRL for acetochlor ESA. A chronic HBV of 50 ug/L was derived in 2006 based on a total UF of 10,000 and an intake adjustment factor of 3. The 2009 HBVs above are based on the 2009 HRL rules methodology (e.g., duration specific intake rates) and revised total uncertainty factor evaluations. As a result, the chronic 2009 HBV is 6-fold higher due to: 1) a decrease in the magnitude of the subchronic-to-chronic UF from 10 to 3; 2) a lower intake rate; and 3) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observations	No	No[2]	No[3]	Yes
Effects?	Yes[1]	--	--	--	Yes[4]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Alterations in thyroid hormone levels were reported at the lowest dose tested in a 28 day range-finding study and form the basis of the Short-term HBV. Alterations in thyroid hormone levels have also been reported for acetochlor OXA and the parent, acetochlor. Thyroid mechanism of action studies conducted on the parent, acetochlor, indicate that acetochlor disrupts thyroid-pituitary homeostasis via increased clearance of serum thyroxin (T4). The Subchronic study did not include an evaluation of thyroid hormone levels. The Subchronic HBV is based on the no adverse effect level (NOAEL) identified in the subchronic study and includes an uncertainty factor for database deficiency to address the need for additional testing on acetochlor ESA regarding altered thyroid hormone levels.

[2] No developmental study has been conducted. Registrant recommended that the OPP consider the alachlor ESA developmental study in rats as evidence that development is not a sensitive endpoint. The developmental study on the parent, acetochlor, identified LOAELs of 400-600 mg/kg-d and NOAELs of 150 – 200 mg/kg-d, based on signs of clinical toxicity and decreased weight gain in pregnant animals, increased resorptions and decreased fetal weights. However, the multiple generation study on the parent identified significantly lower NOAEL/LOAEL values (21-22/66-71 mg/kg-d), indicating that the standard developmental study protocol is not a sensitive test. A database uncertainty factor was incorporated into the derivation of the RfD, in part, due to the lack of a multigeneration reproductive study.

[3] Male reproductive toxicity (testicular degeneration and decreased testes weight) was a critical effect for the parent, acetochlor. Alterations in testes weights were reported in the short-term range finding study but not in the 90 day study. A database uncertainty factor was incorporated into the derivation of the RfD, in part, due to concerns that additional testing should be conducted.

[4] A functional observation battery for neurotoxicity was conducted and histopathology of the sciatic nerve was assessed in a 90 study for general toxicity. There were possible signs of neurotoxicity, but none showed dose dependency. Neurological effects were a sensitive endpoint for the parent, acetochlor. A database uncertainty

factor was incorporated into the derivation of the subchronic and chronic RfDs, in part, due to concerns that additional testing should be conducted.

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: July 2009
Expiration Date: July 2014

Chemical Name: Acetochlor OXA
CAS: 184992-44-4
Synonyms: Acetochlor Oxanilate Metabolite, R290130

Acute Non-Cancer Health-Based Value ($nHBV_{acute}$) = Insufficient data

Short-term Non-Cancer HBV ($nHBV_{short\text{-}term}$) = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.12 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 208 rounded to **200 ug/L**

Reference Dose:	0.12 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	370 mg/kg-d (LOAEL, MRID 45300506 as cited by EPA 2000a and 2006b)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	3000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 10 LOAEL-to-NOAEL, 3 for database insufficiency (lack of multigenerational reproductive study)
Critical effect(s):	Dose-related decrease in body weight gain, thyroid stimulating hormone (TSH), and total iodothyronine (tT3); increased relative thyroid weight
Co-critical effect(s):	None
Additivity endpoint(s):	Thyroid (E) (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Subchronic Non-Cancer HBV ($nHBV_{subchronic}$) = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.077 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 200 ug/L

Reference Dose:	0.077 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	77.2 mg/kg-d (NOAEL, MRID 45313805 as cited by EPA 2000 and 2006)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	1000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive study; insufficient studies for neurological and endocrine effects; lack of studies in a second species)
Critical effect(s):	Decreased food utilization, adult body weights and body weight gains
Co-critical effect(s):	Alterations in serum thyroid hormone levels
Additivity endpoint(s):	Thyroid (E) (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Chronic Non-Cancer HBV ($nHBV_{chronic}$) = 100 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.026 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 121 rounded to **100 ug/L**

Reference Dose:	0.0257 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	77.2 mg/kg-d (NOAEL, MRID 45313805 as cited by

	EPA 2000 and 2006)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	3,000
UF allocation:	10 for inter species extrapolation, 10 for intra species variation, 10 for database insufficiency (lack of multigenerational reproductive or developmental studies; insufficient studies for neurological and endocrine effects; lack of studies in a second species (dogs have been shown to be more sensitive)), and 3 for use of a subchronic study (based on consideration of a comparison of the 28 and 90 day studies, however, this comparison was considered inadequate to completely remove this UF).
Critical effect(s):	Decreased food utilization, adult body weights and body weight gains
Co-critical effect(s):	Alterations in serum thyroid hormone levels
Additivity endpoint(s):	Thyroid (E) (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	None

Cancer HBV (cHBV) = Not Applicable

Cancer classification:	Acetochlor OXA has not been classified as to its carcinogenic potential. However, EPA has indicated that it is unlikely to be carcinogenic (EPA 2004, EPA 2006b). The parent, acetochlor, is classified as "likely" to be carcinogenic and is considered to be a nonlinear carcinogen (i.e., there is a threshold level of exposure below which there is no cancer risk).

Volatile: No

Summary of changes since 1993/1994 HRL promulgation:
An HRL has not been established for acetochlor OXA. A chronic HBV of 50 ug/L was derived in 2006 based on a total UF of 10,000 and an intake adjustment factor of 3. The 2009 HBVs above are based on the 2009 HRL rules methodology (e.g., duration specific intake rates) and revised total uncertainty factor evaluations. As a result, the chronic 2009 HBV is 2-fold higher due to: 1) a lower POD; 2) a decrease in the magnitude of the

subchronic-to-chronic UF from 10 to 3; 3) a lower intake rate; and 4) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observations	No	Yes	No[3]	Secondary Observations
Effects?	Yes[1]		No[2]		Yes[4]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Alterations in thyroid hormone levels were reported at the lowest dose tested in a 28 day range-finding study and form the basis of the Short-term HBV. Alterations in thyroid hormone levels have also been reported for acetochlor ESA and the parent, acetochlor. Thyroid mechanism of action studies conducted on the parent, acetochlor, indicate that acetochlor disrupts thyroid-pituitary homeostasis via increased clearance of serum thyroxin (T4). The Subchronic study did not include an evaluation of thyroid hormone levels. The Subchronic HBV is based on the no adverse effect level (NOAEL) identified in the subchronic study and includes an uncertainty factor for database deficiency to address the need for additional testing on acetochlor OXA regarding altered thyroid hormone levels.

[2] A single developmental study has been conducted. No adverse developmental effects were reported at the highest dose tested. An increase in maternal mortality was observed in this study. Based on data for the parent, acetochlor, the 2 generation study reported significantly lower NOAEL/LOAEL value than the developmental study indicating that the standard developmental study protocol is not a sensitive test.

[3] Male reproductive toxicity was a critical effect for the parent, acetochlor. The database uncertainty factor was, in part, applied to address the absence of a 2 generational reproductive study.

[4] A dose-dependent increase in motor activity in males was observed in a 90 day study, however, this parameter was highly variable and only reached statistical significance ($p<0.01$) at the highest dose level. Researchers reported, but did not substantiate, that observations were within the range of historical controls. The nervous system has been identified as a chronic critical effect for the parent, acetochlor. The uncertainty factor for database deficiency is applied to the subchronic and chronic RfDs, in part, due to concerns that additional testing should be conducted.

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: April, 14, 2010
Expiration Date: April 2015

Chemical Name: Acetone
CAS: 67-64-1
Synonyms: propanone, β-ketopropane, dimethyl ketone, dimethylformaldehyde, DMK, 2-propanone, propan-2-one

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = 9000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(5 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 8561 rounded to **9000 ug/L**

Reference Dose / Concentration:	5.0 mg/kg-day (laboratory animal - rats)
Source of toxicity value:	MDH 2010
Point of Departure:	1485 mg/kg-d (NOAEL, Dietz, et al. 1991; NTP, 1991)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	300
UF allocation:	UF of 10 was applied to account for intraspecies variation; for interspecies extrapolation, 3 was used for toxicokinetic differences; the toxicodynamics component was 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic effects. Studies show that both humans and rodents metabolize acetone, at low doses, in the liver and by extrahepatic pathway followed by excretion at a higher concentration. UF of 10 was used to account for

	database uncertainty. The database lacks a multigenerational study and adequate studies of the oral neurotoxicity, developmental and developmental neurotoxicity.
Critical effect(s):	Increased kidney weight (consistent with nephropathy seen in rats during the 13-week Dietz study)
Co-critical effect(s):	None
Additivity endpoint(s):	Renal (kidney) system
Secondary effect(s):	Bone marrow effects; centrilobular hepatocellular hypertrophy (liver effects); decreased survival, decreased reproductive index, and increased gestation duration (reproductive effects)

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = 8000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(3 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 7792 rounded to **8000 ug/L**

Reference Dose / Concentration:	3.0 mg/kg-day (laboratory animal - rats)
Source of toxicity value:	MDH 2010
Point of Departure:	900 mg/kg-d (NOAEL, Dietz, et al. 1991; NTP, 1991)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	300
UF allocation:	UF of 10 was applied to account for intraspecies variation; for interspecies extrapolation, 3 was used for toxicokinetic differences; the toxicodynamics component was 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic effects. Studies show that both humans and rodents metabolize acetone, at low doses, in the liver and by extrahepatic pathway followed by excretion at a higher concentration. UF of 10 was used to account for database uncertainty. The database lacks a

	multigenerational study and adequate studies of the oral neurotoxicity, developmental and developmental neurotoxicity. Additionally, the database uncertainty factor also accounts for non-biologically significant changes and inconsistent dose-responses in hematological parameters at doses ≤ 900 mg/kg-day that may be indicative of precursor events for development of hematological toxicity (i.e., macrocytic anemia).
Critical effect(s):	Nephropathy – Renal (kidney) system, changes in hematological (blood) parameters consistent with bone marrow toxicity
Co-critical effect(s):	Tubular degeneration of kidneys - renal (kidney system)
Additivity endpoint(s):	Renal (kidney) system, Hematological (blood) system
Secondary effect(s):	Increased testes weights, decreased sperm motility, increased incidence of abnormal sperm, and depressed caudal weight (Reproductive effects); excessive salivation (neurological)

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = 4000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.9 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 4186 rounded to **4000 ug/L**

Reference Dose / Concentration:	0.90 mg/kg-day (laboratory animal -rats)
Source of toxicity value:	MDH 2010 (same as EPA, IRIS 2003)
Point of Departure:	900 mg/kg-d (NOAEL, Dietz, et al. 1991; NTP, 1991)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	1000
UF allocation:	UF of 10 was applied to account for intraspecies; for interspecies extrapolation, 3 was used for toxicokinetic differences; the toxicodynamics component was 1 because humans are not anticipated to be more susceptible than rats to the nephrotoxic

effects. Studies show that both humans and rodents metabolize acetone, at low doses, in the liver and by extrahepatic pathway followed by excretion at a higher concentration. UF of 10 was used to account for database uncertainty. The database lacks a multigenerational study and adequate studies of the oral neurotoxicity, developmental and developmental neurotoxicity. Additionally, the database uncertainty factor also accounts for non-biologically significant changes and inconsistent dose-responses in hematological parameters at doses ≤ 900 mg/kg-day that may be indicative of precursor events for development of hematological toxicity (i.e., macrocytic anemia). The database contains oral subchronic studies but lacks chronic studies. A subchronic to chronic uncertainty factor of 3 is used due to uncertainty about increased severity of effects from increased duration of oral exposure to acetone. Based on information provided in the IRIS summary, a value of 3 rather than 10 is justified because effects from chronic exposure to acetone are not likely to be dramatically different than during subchronic exposure because acetone is produced endogenously, there are multiple pathways of acetone elimination – excretion, exhalation, and metabolism – and acetone does not accumulate in the body.

Critical effect(s):	Nephropathy – Renal (kidney) system, changes in hematological (blood) parameters consistent with bone marrow toxicity
Co-critical effect(s):	Tubular degeneration of kidneys - renal (kidney system).
Additivity endpoint(s):	Renal (kidney) system, Hematological (blood) system, Neurological effects
Secondary effect(s):	Increased testes weights, decreased sperm motility, increased incidence of abnormal sperm, and depressed caudal weight (Reproductive effects); excessive salivation (neurological)

Cancer Health Risk Limit (cHRL) = Not Applicable

Cancer classification:	No cancer classification is available for acetone
Slope factor:	Not applicable

Source of slope factor: Not applicable
Tumor site(s): Not applicable

Volatile: Yes (moderate volatility)

Summary of changes since 1993/1994 HRL promulgation:
The $HBV_{chronic}$ (4000 µg/L) is approximately 6 times higher than the 1993/94 HRL value (700 µg/L) as the result of : 1) utilizing more recent intake rates which incorporate higher intake rates during early life, 2) a 9-fold increase in the RfD value, and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	Yes	Yes	Yes – Secondary Observations	Yes
Effects?	-	No	Yes[1]	Yes[2]	Yes[3]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:
[1] Decreased pup survival was observed after pregnant rats were exposed to acetone at 3500 mg/kg-day by oral gavage which is 1.5 times higher than the short-term LOAEL of 2328 mg/kg-day (EHRT 1987 as cited by ATSDR 1994). Offspring exposed to acetone through inhalation during gestation experienced decreased fetal weight and increased incidence of fetal malformations. During another developmental inhalation study in mice, no developmental effects were seen in the offspring (Mast et al, 1988).
[2] Reproductive effects from exposure to acetone observed during an oral gavage study in pregnant rats included a decreased reproductive index and increase in the gestation duration at 3500 mg/kg-day (EHRT 1987 as cited by ATSDR 1994). Male rats exposed to acetone through drinking water for 13 weeks experienced an increase in relative testes weight, decreased caudal and epididymal weights, depressed sperm motility, and increased incidence of abnormal sperm at 3400 mg/kg-day (decreased testes weights could have been due to an overall decrease in body weight) (Dietz 1991). No reproductive effects were seen when male rats exposed to acetone in drinking water for 6-week prior to mating (Larsen et al. 1991). The reproductive effects observed in both studies occurred at approximately 1.5 times the short-term LOAEL of 2328 mg/kg-day

and approximately 2 times higher than the subchronic/chronic LOAEL of 1700 mg/kg-day.

[3] A couple of neurotoxicity studies were conducted for oral exposure to acetone with only one reporting very minimally evoked visual potentials in rats at 650 mg/kg-day (approximately 3 times lower than the subchronic/chronic LOAEL of 1700 mg/kg-day). Excessive salivation was also observed in rats exposed to acetone in drinking water at 2500 mg/kg-day (1.5 times the subchronic/chronic LOAEL of 1700 mg/kg-day). Narcotic-like effects have been reported after humans have inhaled or ingested acetone which include lethargy, minimal responsiveness, and comatose condition. Excessive salivation has also been observed in animals following acetone ingestion. Neurotoxicity observed in animals following inhalation of acetone include: inhibition of avoidance behavior, effects on fixed ratio and fixed interval response rates, and central nervous system depression measured by tests of unconditioned performance and reflexes.

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: July 2009
Expiration Date: July 2014

Chemical Name: Dichlorodifluoromethane

CAS: #75-71-8

Synonyms: Freon 12 (CFC-12)

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = Insufficient data

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = Insufficient data

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = Insufficient data

Chronic Non-Cancer Health Based Value (nHBV) = 700 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.15 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 698 ug/L rounded to **700ug/L**

Reference Dose:	0.15 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2008 (same as EPA IRIS 1995)
Point of Departure:	150 mg/kg-d (LOAEL based on a 2 year feeding study in rats, Sherman, H. 1974—Haskell Lab as cited by EPA-IRIS 1995)
Human Equivalent Dose Adjustment:	Insufficient information
Total uncertainty factor:	1000
UF allocation:	10 interspecies extrapolation from animal to human; 10 intraspecies variation. The NOAEL was an order of magnitude lower than the minimal effect LOAEL.

Rather than use the NOAEL the minimal LOAEL was used with a LOAEL-to-NOAEL UF of 3. A database UF of 3 was also used to address insufficiencies (lack of developmental study and lack of detailed study information).

Critical effect(s): Decreased body weight
Co-critical effect(s): None
Additivity endpoint(s): None
Secondary effect(s): None

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification: Group D not classifiable as to human carcinogenicity (EPA 2006)

Volatile: Yes (highly volatile)

Summary of changes since 1993/1994 HRL promulgation:
The chronic HBV (700 ug/L) is 1.4 fold lower than the 1993/94 HRL (1000 ug/L) as the result of: 1) incorporating a time-weighted average intake rate which incorporates higher intake rates early in life; 2) utilization of a slightly lower RfD; and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Developmental	Reproductive	Neurotoxicity
Tested?	No	No	No	Yes	Yes
Effects?	--	--	--	No[1]	Yes[2]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] EPA 1995 (IRIS) reported that no effects were observed in a three generation study, however, no study details (e.g., dose levels, parameters evaluated) were included in the EPA summary.

[2] Behavioral neurotoxicity has been studied in animals exposed via inhalation, and has been observed in humans in cases of abuse (huffing) and in occupational studies.

Exposures in inhalation studies have not been compared to exposures in feeding studies.

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: May 2009
Expiration Date: May 2014

Chemical Name: 1,1-Dichloroethylene

CAS: 75-35-4

Synonyms: Vinylidene chloride

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = Not Derived (Insufficient data)

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = Not Derived (Insufficient data)

Subchronic Health Based Value ($nHBV_{subchronic}$) = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.09 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 233 rounded to **200 ug/L**

Reference Dose / Concentration:	0.09 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	9 mg/kg-d (NOAEL, Nitschke et al 1983 with support from Quast et al 1977 and 1983)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability
Critical effect(s):	Fatty changes in the liver
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system
Secondary effect(s):	None

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.046 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 214 rounded to **200 ug/L**

Reference Dose / Concentration:	0.046 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	4.6 mg/kg-d ($BMDL_{10}$, Quast et al 1983)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability
Critical effect(s):	Fatty changes in the liver
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system
Secondary effect(s):	Increased liver weight and enzyme activity

Cancer Transition Health Based Value ($cHBV_{cancer}$) = "Not Applicable"

Cancer classification:	Inadequate for assessment of human carcinogenic potential by the oral route, based on the absence of statistically or biologically significant tumors in limited bioassays in rats and mice balanced against the suggestive evidence in male mice in a single bioassay by inhalation and limited evidence of genotoxicity (EPA 2002)
Slope factor:	NA
Source of slope factor:	NA
Tumor site(s):	NA

Volatile: Yes (highly volatile)

Summary of changes since 1993/1994 HRL promulgation:
The subchronic and chronic nHBV (200 ug/L) is approximately 33 times higher than the 1993/94 HRL (6 ug/L) as the result of: 1) a nearly 6 fold increase in the RfD due to a reassessment of toxicity; 2) carcinogenicity re-classification (resulting in the removal of the 10 fold uncertainty factor for Class C); and 3) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute

	Endocrine	Immunotox	Development	Reproductive	Neurotoxicity
Tested?	No[1]	No[1]	Yes	Yes	Yes
Effects?	--	--	Yes[2]	Yes[2]	No[3]

Lack of testing specific for a health effect does not necessarily imply that the toxicity value is not protective of the health effect. Most chemicals have been subject to a number of studies in which researchers identify those effects that occur at the lowest doses; subsequent testing is done to narrow in on the threshold dose for those effects.

Comments on extent of testing or effects:
[1] No focused studies on endocrine or immune effects have been performed; however, the existing bioassays provide no evidence of effects.
[2] Two developmental and 1 three generational reproductive oral studies have conducted. No developmental or reproductive effects were observed in these studies. The highest dose tested was approximately 4-fold higher than the chronic critical study LOAEL. Developmental effects have been observed in inhalation studies, however, maternal toxicity was typically evident at the levels that resulted in developmental toxicity. Inhalation studies also indicate that the liver is the most sensitive organ.
[3] A single inhalation neurodevelopmental toxicity study has been conducted and although there was evidence of maternal and developmental toxicity (e.g., weight loss) no effects were observed in behavioral tests. There are no other focused studies on neurotoxicity, however, there is no indication from chronic, reproductive, and developmental bioassays in rats and mice by oral or inhalation exposure that neurotoxicity is a sensitive endpoint.

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: February 18, 2010
Expiration Date: February 2015

Chemical Name: Ethylbenzene
CAS: 100-41-4
Synonyms: Ethylbenzol, EB, phenylethane

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = Not Derived (Insufficient Data)

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = 50 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term Intake Rate L/kg/d)}}$$

$$= \frac{\text{(0.075 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 51.9 rounded to **50 ug/L**

Reference Dose:	0.075 (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	75 mg/kg-d (NOAEL based on Mellert et al, 2007)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	1000
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability, 10 for database deficiencies (to address concerns regarding lack of oral studies of developmental and reproductive toxicity, lack of toxicity data in more than 1 species, as well as limited evidence of otoxicity that may be relevant to the oral route of exposure).
Critical effect(s):	Changes in liver and kidney weights (with histological changes; and blood chemistry changes at higher doses)
Co-critical effect(s):	None

Additivity endpoint(s):	Hepatic (liver) system, Renal (kidney) system
Secondary effect(s):	None

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = ($nHBV_{short-term}$) = 50 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.048 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 124 rounded to 100 ug/L

Reference Dose / Concentration:	0.048 (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	48 mg/kg-d ($BMDL_{10}$, EPA 2009 based on Mellert et al, 2007)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	1000
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability, 10 for database deficiencies (to address concerns regarding lack of oral studies of developmental and reproductive toxicity, lack of toxicity data in more than 1 species, as well as limited evidence of otoxicity that may be relevant to the oral route of exposure).
Critical effect(s):	Changes in liver (with histological changes; and blood chemistry changes at higher doses)
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system
Secondary effect(s):	Renal (kidney) system

The Subchronic nHRL must be protective of the short-term exposure that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 50 ug/L. Additivity Endpoints: Liver System and Kidney System

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = ($nHBV_{short\text{-}term}$) = 50 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate L/kg/d)}}$$

$$= \frac{\text{(0.016 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 74.4 rounded to 70 ug/L

Reference Dose / Concentration:	0.016 (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	48 mg/kg-d ($BMDL_{10}$, EPA 2009 based on Mellert et al, 2007)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	3000
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability, 3 for subchronic-to-chronic extrapolation (database does not contain a chronic study and the liver effects were observed at a lower dose in the 90-day study than in the 28-day study (Mellert et al, 2007), and 10 for database deficiencies (to address concerns regarding lack of oral studies of developmental and reproductive toxicity, lack of toxicity data in more than 1 species, as well as limited evidence of otoxicity that may be relevant to the oral route of exposure).
Critical effect(s):	Changes in liver and kidney weights (with histological changes; and blood chemistry changes at higher doses)
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system
Secondary effect(s):	Renal (kidney) system

The Chronic nHRL must be protective of the short-term exposure that occur within the chronic period and therefore, the Chronic nHBV is set equal to the Short-term nHBV of 50 ug/L. Additivity Endpoints: Liver System and Kidney System

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	D; not classifiable as to human carcinogenicity (EPA IRIS, 1991).
Slope factor:	None
Source of slope factor:	None
Tumor site(s):	None

Volatile: Yes (highly)

Summary of changes since 1993/1994 HRL promulgation:
The short-term, subchronic and chronic HBVs (50 ug/L) are 14-fold lower than the 1993/94 HRL value (700 ug/L) as the result of : 1) more recent toxicity studies; 2) a multi-duration assessment and utilization of higher intake rates; and 3) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observation	Secondary Observation	Yes	Yes	Yes
Effects?	Yes[1]	Yes[2]	Yes[3]	No	Yes[4]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:
[1] No oral endocrine studies available. There is an available reproduction study reported that acute oral exposure to 500 or 1,000 mg/kg ethylbenzene decreases peripheral hormone levels and may block or delay the estrus cycle in female rats during the diestrus stage (Ungváry 1986).

[2] No oral immunotoxicity studies were found. Observations reported in a 90-day rat study include a significant decrease in absolute and relative thymus in females treated with ≥250 mg/kg/day for 13 weeks, but no histopathological findings were observed (Mellert et al. 2007).
[3] There are no oral developmental studies. There are several inhalation developmental studies. Results of studies in rats indicate that ethylbenzene produces reduced fetal

weight, skeletal anomalies, and anomalies and delayed development of urogenital tract; skeletal and urogenital anomalies were observed in the presence of maternal toxicity (Faber et al. 2006; NIOSH 1981; Ungváry and Tátrai 1985).

[4] Significant ototoxic effects were observed in male rats administered 900 mg/kg/day (the only dose tested) by gavage for 2 weeks (Gagnaire and Langlais 2005). The authors reported an almost complete loss of the three rows of OHCs in the organ of Corti 10 days after the last exposure to ethylbenzene.

In male and female rats exposed to 75–750 mg/kg/day ethylbenzene by gavage for 13 weeks, no neurological effects were observed, based on negative results of motor activity (note: female rats did show increased motor activity at the highest dose tested) tests and a functional observational battery (FOB) (Mellert et al. 2007).

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2009 Health Based Guidance Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: March 12, 2010
Expiration Date: March 2015

Chemical Name: Ethylene Glycol
CAS: 107-21-1
Synonyms: Ethane-1,2-diol; Monoethylene glycol (MEG); 1,2-Ethanediol; Glycol

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = 4,000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Acute intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.756 mg/kg/d) x (0.2)* x (1000 ug/mg)}}{\text{(0.043 L/kg-d)*}}$$

= 3,516 rounded to **4,000 ug/L**

* the RfD is based on malformations that occur *in utero*, therefore the intake rate for a pregnant women is utilized rather than the default infant intake rate as described in the SONAR (page 46). Effects relevant to post-natal development (e.g., body weight) occurred at higher dose levels. Since the acute duration intake is based on pregnant women, not infants, an RSC of 0.2 is utilized.

Reference Dose / Concentration:	0.756 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	75.6 mg/kg-d ($BMDL_{10}$ for skeletal malformations in mice calculated by ATSDR 2007 based on data from Neeper-Bradley et al 1995. NOAEL/LOAEL were 150/500 mg/kg-d)
Human Equivalent Dose Adjustment:	Insufficient data for adjustment
Total uncertainty factor:	100
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability
Critical effect(s):	Increased incidence of skeletal malformations
Co-critical effect(s):	None
Additivity endpoint(s):	Development
Secondary effect(s):	Decreased fetal and pup body weights, decreased

	embryo/fetal viability, renal lesions

Short-term Non-Cancer Health Based Value (nHBV$_{short-term}$) = 4,000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.756 mg/kg/d) x (0.2)* x (1000 ug/mg)}}{\text{(0.043 L/kg-d)*}}$$

= 3,516 rounded to **4,000 ug/L**

* the RfD is based on malformations that occur *in utero*, therefore the intake rate for a pregnant women is utilized rather than the default infant intake rate as described in the SONAR (page 46). Effects relevant to post-natal development (e.g., body weight) occurred at higher dose levels. Since the short-term duration intake is based on pregnant women, not infants, an RSC of 0.2 is utilized.

Reference Dose / Concentration:	0.756 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	75.6 mg/kg-d ($BMDL_{10}$ for skeletal malformations in mice calculated by ATSDR 2007 based on data from Neeper-Bradley et al 1995. NOAEL/LOAEL were 150/500 mg/kg-d)
Human Equivalent Dose Adjustment:	Insufficient data for adjustment
Total uncertainty factor:	100
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability
Critical effect(s):	Increased incidence of skeletal malformations
Co-critical effect(s):	None
Additivity endpoint(s):	Development
Secondary effect(s):	Decreased fetal and pup body weights, decreased embryo/fetal viability, renal lesions

Subchronic Non-Cancer Health Based Value (nHBV$_{subchronic}$) = 2,000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.715 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 1,857 rounded to **2,000 ug/L**

Reference Dose / Concentration:	0.715 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	71.5 mg/kg-d ($BMDL_{10}$ based on nephropathy by Cruzan et al 2004. NOAEL/LOAEL were 150/500 mg/kg-d)
Human Equivalent Dose Adjustment:	Insufficient data for adjustment
Total uncertainty factor:	100
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability
Critical effect(s):	Decreased adult body weight; increased water intake resulting in lower urine specific gravities and higher urine volumes; increased kidney weight; increased calcium oxalate crystals in kidney tubules and crystal nephropathy.
Co-critical effect(s):	Increased incidence of skeletal malformations in fetuses exposed *in utero*
Additivity endpoint(s):	Renal (kidney) system, Development
Secondary effect(s):	Decreased fetal and pup body weights, decreased embryo/fetal viability. Adult animals - increased incidence renal lesions and increased mortality.

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = 2,000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.5 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 2326 rounded to **2,000 ug/L**

Reference Dose / Concentration:	0.5 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	150 mg/kg-d (NOAEL based on kidney changes reported by Corley et al 2008. LOAEL was 300 mg/kg-d)
Human Equivalent Dose Adjustment:	Insufficient data for adjustment

Total uncertainty factor:	300
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability, 3 for subchronic-to-chronic UF (comparison of the 16 week (Cruzan et al 2004) and 12 month study (Corley et al 2008) suggests increased severity with increased duration, however, since the study is 12 months in length a factor of 3 rather than 10 was used)
Critical effect(s):	Decreased adult body weight; increased water intake resulting in lower urine specific gravities and higher urine volumes; increased kidney weight; gross and histological changes in kidney and bladder.
Co-critical effect(s):	Increased incidence of skeletal malformations in fetuses exposed *in utero*
Additivity endpoint(s):	Renal (kidney) system; Development (skeletal malformations)
Secondary effect(s):	Decreased fetal/pup body weight; decreased embryo/fetal viability; increased pre-implantation loss; Decreased adult body weight; proteinurea; decreased testis weight and sperm count; increased incidence of renal lesions; and increased mortality

Cancer Health Based Value (cHBV) = "Not Applicable"

Cancer classification:	Not available. Ethylene glycol has not undergone a complete evaluation and determination by EPA for evidence of human carcinogenic potential. (EPA 1989)
Slope factor:	Not available

Volatile: No

Summary of changes since 1993/1994 HRL promulgation:
The 1993/94 noncancer HRL was 10,000 ug/L. The Acute and Short-term HBV values of 4,000 ug/L and Subchronic and Chronic HBV values of 2,000 ug/L are 2.5- and 5-fold, respectively, lower as a result of incorporating: 1) a more recent evaluation of the toxicity information, 2) updated intake rates that include higher intake rates in children, and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No[1]	No[2]	Yes	Yes	Yes
Effects?	-	-	Yes[3]	Yes[4]	Yes[5]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] No studies. Secondary observations from histological examinations of endocrine organs in existing studies of ethylene glycol showed no effects in rats or mice, however, none of these studies included assessments of endocrine function.

[2] No studies. Secondary observations from histological examinations of immune and lymphoreticular system tissues in existing studies of ethylene glycol showed no effects in rats or mice, however, none of these studies included assessments of immune function.

[3] Numerous developmental studies have been conducted. Mice have been shown to be more sensitive than rats or rabbits regarding developmental effects. The acute and short-term RfD is based on skeletal malformations observed in mouse fetuses following exposure *in utero*. Development (skeletal malformations) have also been identified as co-critical effects for subchronic and chronic duration. As doses increase additional effects (decreased fetal/pup body weight, decreased embryo/fetal viability) are also observed. These additional effects have been identified as secondary effects.

[4] Reproductive and multi-generation studies have been conducted. Decreased litters/mating pair, increased pre- and post-implantation loss, decreased sperm were observed at dose levels approximately 2 to 3-fold higher than the acute, short-term, subchronic and chronic duration LOAELs. As a result these effects have been identified as secondary effects for the acute, short-term, subchronic and chronic durations.

[5] Following acute ingestion (poisoning incidents) of very high doses ethylene glycol has a direct toxic effect on the nervous system (ataxia, convulsions, coma). At lower doses in mature animals, calcium oxalate crystals have been observed. However, these doses were 5 to 10-fold higher than the LOAELs identified for the acute, short-term, subchronic and chronic durations.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: May 2009
Expiration Date: May 2014

Chemical Name: Metolachlor and S-Metolachlor
CAS # : 51218-45-2 and 87392-12-9
Synonyms: Dual; Pennant; Primagram; Primextra; Turbo

Acute/Short-term Non-Cancer Health Based Value ($nHBV_{acute/short-term}$) = 400 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Acute/short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.24 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 415.2 rounded to **400 ug/L**

Reference Dose:	0.24 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	23.5 mg/kg-d (NOAEL, based on a 2 generation rat study by Smith et al, 1981 (Ciba-Geigy) as cited by EPA 1994 & 1995)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 fold for interspecies extrapolation and 10 for intraspecies variability
Critical effect(s):	reduced pup weights
Co-critical effect(s):	None
Additivity endpoint(s):	Developmental (decreased body weight)
Secondary effect(s):	None

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = 300 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic, L/kg/d)}}$$

$$= \frac{\text{(0.097 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 251.9 rounded to **300 ug/L**

Reference Dose:	0.097 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	9.7 mg/kg-d (NOAEL, based on a 1 year dog study, MRID 409807-01 as cited by EPA 1995 & 2002)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 fold for interspecies extrapolation and 10 for intraspecies variability
Critical effect(s):	Decreased body weight in adult
Co-critical effect(s):	None
Additivity endpoint(s):	None (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	Decreased body weight in pups

Chronic Non-Cancer Health based Value ($nHBV_{chronic}$) = 300 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.097 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 451.2 rounded to 500 ug/L

Reference Dose:	0.097 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	9.7-mg/kg-d (NOAEL, based on a 1 year dog study, MRID 409807-01 as cited by EPA 1995 & 2002)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	100
UF allocation:	10 fold for interspecies extrapolation and 10 for

	intraspecies variability. (Based on comparison of effects observed after various durations of exposure the application of a subchronic-to-chronic UF was determined to be unnecessary)
Critical effect(s):	Decreased body weight in adult
Co-critical effect(s):	None
Additivity endpoint(s):	None (Body weight effects in adults are not utilized for additivity)
Secondary effect(s):	Decreased body weight in pups; increased liver weight

The Chronic nHBV must be protective of the subchronic exposures that occur within the chronic period and therefore, the Chronic nHBV is set equal to the Subchronic nHBV of 300 ug/L. Additivity Endpoints: None.

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	Group C "possible human carcinogen" Nonlinear approach recommended (EPA 1995, 2002, 2006)
Slope factor:	None
Source of slope factor:	None
Tumor site(s):	Liver

The chronic RfD (0.097 mg/kg-d) is protective for cancer risk.

Volatile: No

Summary of Guidance Value History:
The acute, short-term, and subchronic nHBVs are new values. The chronic nHBV (300 ug/L) is higher than the 1993/94 nHRL (100 ug/L), due to: 1) the removal of the group C factor, 2) more recent intake rates which incorporate higher intake rates during early life, and 3) the value has been rounded to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No[1]	No	Yes	Yes	No[3]
Effects?	--	--	Yes[2]	Yes[2]	--

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Not tested. Increased relative thyroid weights were observed in F1 males in the multigenerational study. Related compound, acetochlor, causes thyroid effects.

[2] Decreased pup weight was observed at the acute/short-term critical study LOAEL and is the basis of the acute & short-term nHBV. These dose levels were ~ 2-3-fold higher than the subchronic and chronic critical study LOAEL. Decreased pup body weight has been listed as a subchronic and chronic secondary endpoint. Reduction in the number of implantations and increased resorptions resulting in decreased litter size have also been reported, but at dose levels greater than 30-fold higher than the acute/short-term, subchronic and chronic critical study NOAELs.

[3] Not tested. Related compound, acetochlor, causes neurological effects.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: May 2009
Expiration Date: May 2014

Chemical Name: Metolachlor ESA
CAS: 171118-09-5
Synonyms: Ethanesulfonate degradate of metolachlor; CGA-354743

Acute Non-Cancer HBV ($nHBV_{acute}$) = Insufficient Data (Not Derived)

Short-term Non-Cancer HBV ($nHBV_{short\text{-}term}$) = Insufficient Data (Not Derived)

Subchronic Non-Cancer HBV ($nHBV_{subchronic}$) = 4000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(1.7 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 4415 rounded to **4000 ug/L**

Reference Dose:	1.7 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	500 mg/kg-d (NOAEL, based on a 90 day subchronic study in dogs, MRID 44931709 Data Evaluation Report submitted to EPA 2001)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	300
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability and 3 database insufficiencies (e.g., lack of a 2 generation reproductive study)
Critical effect(s):	Increased levels of serum liver enzymes and statistically significant trend in increased liver weight.
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system

Secondary effect(s):	None

Chronic Non-Cancer HBV (nHBV$_{chronic}$) = 800 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(0.17 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 790 rounded to **800 ug/L**

Reference Dose:	0.17 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	500 mg/kg-d (NOAEL, based on a 90 day subchronic study in dogs, MRID 44931709 a Data Evaluation Report submitted to EPA 2001)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	3000
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability, 10 use of a subchronic study (inadequate information for comparing effects across exposure duration - default value was used), and 3 database insufficiencies (e.g., lack of a 2 generation reproductive study)
Critical effect(s):	Increased levels of serum liver enzymes and statistically significant trend in increased liver weight.
Co-critical effect(s):	None
Additivity endpoint(s):	Hepatic (liver) system
Secondary effect(s):	None

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	information on carcinogenicity is unavailable[1]
Slope factor:	None
Source of slope factor:	None
Tumor site(s):	Unavailable

[1]Nonlinear approach is recommended for the parent compound (metolachlor). MDH considers the RfD protective of cancer.

Volatile: No

Summary of Guidance Value History:
There is no 1993/94 HRL for metolachlor ESA. The chronic nHBV (800 ug/L), is slightly lower than the HBV issued in 2004 (1000 ug/L) due to: 1) incorporation of a database uncertainty factor; 2) utilization of a lower intake rate; and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No[1]	Yes	No[2]	No
Effects?	--	--	No[2]	--	--

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:
The database for metolachlor ESA is limited (one developmental study in rats, one subchronic study in rats and one subchronic study in dogs). The database for the parent compound (metolachlor) is comprehensive and includes reproductive, numerous developmental, and chronic (oncogenicity) studies.

[1] Dermal sensitization studies have been done, and some sensitization is observed. However, there is no indication of toxicity to the immune system.
[2] The single available developmental study reported no treatment related effects to pregnant animals or fetuses at the highest dose tested. This dose level is higher than the critical study LOAEL. The database for the parent compound demonstrated that developmental toxicity observed in the 2 generation reproductive study occurred at lower doses than the standard developmental study. No 2 generation reproductive study has been conducted for metolachlor ESA. A database uncertainty factor was incorporated into the RfD derivation to address this data gap.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: May 2009
Expiration Date: May 2014

Chemical Name: Metolachlor OXA
CAS: 152019-73-3
Synonyms: (Oxanilic acid degradate of metolachlor)

Acute Non-Cancer HBV ($nHBV_{acute}$) = Insufficient Data (Not Derived)

Short-term Non-Cancer HBV ($nHBV_{short\text{-}term}$) = 3000 ug/L

$$\frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(1.7 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 2941 rounded to **3000 ug/L**

Reference Dose:	1.7 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	500 mg/kg-d (NOAEL based on a 90 day dog feeding study submitted to MDH by Syngenta (6/23/2004)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	300
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability, and 3 for database insufficiencies (e.g., lack of a 2 generation reproductive study)
Critical effect(s):	Changes in blood chemistry but unable to identify specific target organ
Co-critical effect(s):	None
Additivity endpoint(s):	None
Secondary effect(s):	None

Subchronic Non-Cancer HBV ($nHBV_{subchronic}$) = Short-term nHBV = 3000 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(1.7 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 4415 rounded to 4000 ug/L

Reference Dose:	1.7 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	500 mg/kg-d (NOAEL based on a 90 day dog feeding study submitted to MDH by Syngenta (6/23/2004)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	300
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability, and 3 for database insufficiencies (e.g., lack of a 2 generation reproductive study)
Critical effect(s):	Changes in blood chemistry but unable to identify specific target organ
Co-critical effect(s):	None
Additivity endpoint(s):	None
Secondary effect(s):	None

The Subchronic nHBV must be protective of the short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 3,000 ug/L. Additivity Endpoints: None.

Chronic Non-Cancer Health based Value ($nHBV_{chronic}$) = 800 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.17 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 790 rounded to **800 ug/L**

Reference Dose:	0.17 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH, 2009
Point of Departure:	500 mg/kg-d (NOAEL based on a 90 day dog feeding study submitted to MDH by Syngenta, 6/23/2004)
Human Equivalent Dose Adjustment:	Insufficient data
Total uncertainty factor:	3000
UF allocation:	10 interspecies extrapolation, 10 intraspecies variability, 10 use of a subchronic study (inadequate information for comparing effects across exposure duration - default value was used), and 3 database insufficiencies (e.g., lack of a 2 generation reproductive study)
Critical effect(s):	Changes in blood chemistry but unable to identify specific target organ
Co-critical effect(s):	None
Additivity endpoint(s):	None
Secondary effect(s):	None

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	Information on carcinogenicity is unavailable[1]
Slope factor:	None
Source of slope factor:	None
Tumor site(s):	Unavailable

[1]Nonlinear approach is recommended for the parent compound (metolachlor). MDH considers the RfD protective of cancer.

Volatile: No

Summary of Guidance Value History:
There is no 1993/94 HRL for metolachlor OX. The chronic nHBV (800 ug/L), is slightly lower than the HBV issued in 2004 (1000 ug/L) due to 1) incorporation of a database uncertainty factor; 2) utilization of a lower intake rate; and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No[1]	Yes[2]	No[2]	No
Effects?	--	--	No	--	--

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

The database for metolachlor OXA is limited (one developmental study in rats, one subchronic study in rats and one subchronic study in dogs). The database for the parent compounds is comprehensive and includes reproductive, numerous developmental, and chronic (oncogenicity) studies.

[1] Dermal sensitization studies have been done, and some sensitization is observed. However, there is no indication of toxicity to the immune system.

[2] The single available developmental study reported no observable effects to pregnant animals or fetuses even at the highest dose tested. This dose level is higher than the critical study LOAEL. The database for the parent compound demonstrated that developmental toxicity observed in the 2 generation reproductive study occurred at lower doses than the teratology endpoints assessed in the standard developmental study. No 2 generation reproductive study has been conducted for metolachlor OA. A database uncertainty factor was incorporated into the RfD derivation to address this data gap.

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EPA Region 3. Risk Based Concentration. (click on RBC Tables PDF link) http://www.epa.gov/reg3hwmd/risk/human/rbc/rbc1006.pdf

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: May 18, 2010
Expiration Date: May 2015

Chemical Name: Perfluorobutyric acid
CAS: 375-22-4
Synonyms: PFBA, Perfluorobutyrate , Heptafluorobutyric acid

Acute Non-Cancer Health-Based Value (HBV_{acute}) = Not Derived*

** While a developmental study is available for PFBA, a human equivalent dose (HED) forms the basis of the reference dose and assumes steady state conditions that cannot be achieved from a one-day exposure. Based on a mean human half-life of 3 days steady-state conditions would be established within ~ 9-15 days. At the present time the information necessary to estimate less than steady-state doses is not available. The short-term HBV assessment incorporated information regarding developmental effects.*

Short-term Non-Cancer Health-Based Value ($HBV_{short\text{-}term}$) = 7 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.0038 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 6.57 rounded to **7 ug/L**

Toxicity value:	0.0038 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2008
Point of Departure:	3.01 mg/kg-d ($BMDL_{10}$, calculated by Butenhoff, 2007 based on NOTOX 2007a 28-day study)
Human Equivalent Dose:	3.01/8 = 0.38 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor:	100
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability, and 3 database insufficiencies (e.g., study did not identify a NOAEL or acceptable $BMDL_{10}$ for thyroid effects. A multigeneration reproductive study has not been

	conducted, however the database does include an extended 1 generation developmental study.)
Critical effect(s):	decreased cholesterol
Co-critical effect(s):	increased relative thyroid weight, decreased serum total thyroxine (TT4) & dialysis free thyroxine (dFT4)
Additivity endpoint(s):	Hepatic (liver) system; Thyroid (E)
Secondary effect(s):	Delayed eye opening

Subchronic Non-Cancer Health-Based Value ($HBV_{subchronic}$) = 7 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.0029 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 7.53 rounded to 8 ug/L

Toxicity value:	0.0029 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2008
Point of Departure:	6.9 mg/kg-d (NOAEL, NOTOX 2007b 90-day study)
Human Equivalent Dose:	6.9/8 = 0.86 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor:	300
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability, and 10 database insufficiencies (e.g., assessment of thyroid effects was compromised by missing serum hormone data. A multigeneration reproductive study has not been conducted, however the database does include an extended 1 generation developmental study.)
Critical effect(s):	liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin
Co-critical effect(s):	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoint(s):	Developmental; Hematologic (blood) system; Hepatic (liver) system; Thyroid (E)
Secondary effect(s):	Increased liver weight and delayed vaginal opening in offspring exposed during gestation

The Subchronic HBV must be protective of short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 7 ug/L. The Additivity endpoints are: Hepatic (liver) system; Thyroid (E).

Chronic Non-Cancer Health-Based Value ($HBV_{chronic}$) = 7 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.0029 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 13.49 rounded to 10 ug/L

Toxicity value:	0.0029 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2008
Point of Departure:	6.9 mg/kg-d (NOAEL, NOTOX 2007b 90-day study)
Human Equivalent Dose:	6.9/8 = 0.86 mg/kg-d (factor of 8 adjusts for half-life duration of 3 days in humans versus 9.22 hours in male rats)
Total uncertainty factor:	300
UF allocation:	3 interspecies toxicodynamic differences, 10 intraspecies variability, and 10 database insufficiencies (e.g., assessment of thyroid effects was compromised by missing serum hormone data. A multigeneration reproductive study has not been conducted, however the database does include an extended 1 generation developmental study.). A subchronic-to-chronic UF was not applied since hepatic effects (and additional hematologic effects) were observed at dose levels similar to those in 28-day study. Concerns regarding the thyroid effects are address by the database UF.
Critical effect(s):	liver weight changes, morphological changes in liver and thyroid gland, decreased TT4, and decreased red blood cells, hematocrit and hemoglobin
Co-critical effect(s):	Increased relative thyroid weight, decreased serum TT4 and dFT4, decreased cholesterol, delayed eye opening
Additivity endpoint(s):	Developmental; Hematologic (blood) system; Hepatic (liver) system; Thyroid (E)
Secondary effect(s):	Increased liver weight and delayed vaginal opening in offspring exposed during gestation

The Chronic HBV must be protective of short-term exposures that occur within the chronic period and therefore, the Chronic nHBV is set equal to the Short-term nHBV of 7 ug/L. The Additivity endpoints are: Hepatic (liver) system; Thyroid (E).

Cancer Health-Based Values (cHBV) = Not Applicable

Cancer classification: Not available
Slope factor: Not available
Source of slope factor: Not applicable
Tumor site(s): Not applicable

Volatile: No

Summary of Guidance Value History:
The draft values for short-term, subchronic and chronic are the same as the 2008 HBV values. An acute (one-day) value of 8 ug/L had been derived in 2008, However, while a developmental study is available for PFBA, a human equivalent dose (HED) forms the basis of the reference dose and assumes steady state conditions that cannot be achieved from a one-day exposure to PFBA. Based on a mean human half-life of 3 days steady-state conditions would be established within ~ 9-15 days. At the present time the information necessary to estimate less than steady-state doses is not available. The short-term HBV assessment incorporated information regarding developmental effects.

The Additivity Endpoints associated with the draft HRL values above also reflect a change from 2008. Additivity Endpoints are based on the identified critical and co-critical effects. The basis of the 2008 additivity endpoints (developmental and blood system effects) are now considered secondary effects for the short-term, subchronic, and chronic based on a comparison of the HEDs at which these effects occur.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	Secondary Observations	No	Yes	No	Secondary Observations
Effects?	Yes[1]	--	Yes[2]	--	No[3]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] Secondary observations, including decreased T4 levels, altered hyperplasia/hypertrophy of the follicular epithelium of the thyroid, and increased thyroid weight were noted in the 28 and 90 day studies. These effects are identified as critical or co-critical effects for the short-term, subchronic and chronic duration HBVs.

[2] Developmental delays were observed in offspring of mice exposed during pregnancy. This effect was observed at a human equivalent dose greater than 2-fold higher than the human equivalent dose upon which the short-term RfD is based. Developmental effects are identified as secondary effects.

[3] No available neurotoxicity studies. Secondary observations reported in the 28 and 90-day studies include delayed bilateral pupillary reflex for males exposed to a dose > 10-fold higher than the BMDL used as the basis of the short-term, subchronic and chronic HBVs. Histopathological assessment of neuronal tissues (including the optic nerve) and motor activity evaluations did not reveal any treatment-related abnormalities.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: August 27, 2009

Chemical Name: Perfluorobutane sulfonate
CAS: 375-73-5
Synonyms: PFBS; Nonafluorobutanesulphonic acid

Acute Noncancer Health Based Value ($nHBV_{acute}$) = Not Derived (Insufficient Data)

Short-term Noncancer Health Based Value ($nHBV_{short\text{-}term}$) = Not Derived (Insufficient Data)

Subchronic* Noncancer Health Based Value ($nHBV_{subchronic}$) = 9 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(0.0042 mg/kg/d) x (0.5) x (1000 ug/mg)}}{\text{(0.245** L/kg-d)}}$$

= 8.57 rounded to **9 ug/L**

* Based on a mean human half-life of 27.7 days for PFBS the time to steady state is 2.7 - 4.5 months. Subchronic is defined as a duration of more than 30 days, up to approximately 10% of a lifetime. Rather than the default subchronic period of 8 years a chemical specific duration of 4 months was used.

** Intake rate used corresponds to the time-weighted average 95th% intake rate over first 4 months of life. Since a young infant intake is used a RSC of 0.5, the default for non-volatiles, is utilized.

Reference Dose:	0.0042 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2009
Point of Departure:	60 mg/kg-d (NOAEL, Leider et al 2009a and York 2003a)
Human Equivalent Dose:	0.42 mg/kg-d (Serum levels were not reported, therefore the administered dose NOAEL, 60 mg/kg-d, was divided by a half-life adjustment factor of 142 for extrapolation from male rats to humans)

Total uncertainty factor:	100
UF allocation:	3 interspecies extrapolation for potential differences in toxicodynamics, 10 intraspecies variability and 3 for database insufficiencies (additional studies regarding neurological and thyroid effects are warranted)
Critical effect(s):	Decreased hemoglobin and hematocrit, histological changes in kidney
Co-critical effect(s):	Increased liver weight with increased incidence of hepatocellular hypertrophy
Additivity endpoint(s):	Hematological (blood) system, Hepatic (liver) system, Renal (kidney) system
Secondary effect(s):	Decreased serum protein, albumin and red blood cell count, increased serum chloride

Chronic Noncancer Health Based Value ($nHBV_{chronic}$) = 7 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic Intake Rate, L/kg/d)}}$$

$$= \frac{\text{(0.0014 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 6.51 rounded to **7 ug/L**

Reference Dose:	0.0014 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2009
Point of Departure:	60 mg/kg-d (NOAEL, Leider et al 2009a and York 2003a)
Human Equivalent Dose:	0.42 mg/kg-d (Serum levels were not reported, therefore the administered dose NOAEL, 60 mg/kg-d, was divided by a half-life adjustment factor of 142 for extrapolation from male rats to humans)
Total uncertainty factor:	300
UF allocation:	3 interspecies extrapolation for potential differences in toxicodynamics, 10 intraspecies variability, 3 for database insufficiencies (additional studies regarding neurological and thyroid effects are warranted), and 3 for use of a subchronic study (database does not contain a chronic study and additional effects (decreased hemoglobin and hematocrit) were noted in the 90 day study (Leider et al 2009a and York 2003a) that were not observed following shorter exposure

	durations)
Critical effect(s):	Decreased hemoglobin and hematocrit, histological changes in kidney
Co-critical effect(s):	Increased liver weight with increased incidence of hepatocellular hypertrophy
Additivity endpoint(s):	Hematological (blood) system, Hepatic (liver) system, Renal (kidney) system
Secondary effect(s):	Decreased serum protein, albumin and red blood cell count, increased serum chloride

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	PFBS has not been classified regarding potential carcinogenicity.
Slope factor:	Not available
Source of slope factor:	Not applicable
Tumor site(s):	Not applicable

Volatile: No

Summary of changes since 1993/1994 HRL promulgation:
There are no pre-existing guidance values for PFBS. The HBVs above represent new values.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	No	Yes	Yes	Secondary Observations
Effects?	-	-	Yes[1]	Yes[2]	Unclear[3]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] An oral developmental study and a 2 generational study have been conducted in rats. Both studies identified a NOAEL for developmental effects 5-fold higher than the critical study NOAEL.

[2] An oral 2 generation study in rats has been conducted. No treatment related effects on female reproductive parameters were noted. Decreased number of spermatids per gram testes and increased incidence of abnormal sperm were noted at doses >15-fold higher than the critical study NOAEL. Mating and fertility parameters were unaffected.

[3] Neurological alterations were reported in the 28-day (Premedia Redfield 2001) but not the 90-day oral study (Leider et al 2009a and York 2003a) in rats. The results from the 28-day study are difficult to interpret. Treated males did differ from control males, however, the decreases in tail flick, rotorod latency and foot splay did not exhibit a dose-response at the doses tested. In contrast, treated females exhibited an increase in rotorod latency. The 90 day study, which included a FOB and motor activity assessment but not a peripheral neuropathy assessment per se, did not report any treatment related effects. A database UF was incorporated into the derivation of the subchronic and chronic RfDs, in part, to address the need for additional neurological testing.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

Web Publication Date: November 25, 2009
Expiration Date: November 2014

Chemical Name: Toluene
CAS: 108-88-3
Synonyms: methyl-Benzene; Methylbenzol; Monomethyl benzene; phenyl methane; Tol; Toluol; tolu-sol

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = Not Derived (insufficient data)

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.22 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.289 L/kg-d)}}$$

= 152 rounded to **200 ug/L**

Reference Dose / Concentration:	0.22 (laboratory animal)
Source of toxicity value:	MDH 2009
Point of Departure:	22 mg/kg-d (NOAEL based on Hsieh et al 1989)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	100
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability
Critical effect(s):	immunosuppression
Co-critical effect(s):	Changes in brain neurotransmitter levels and decreased open field activity
Additivity endpoint(s):	Immune system, Nervous system
Secondary effect(s):	None

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = $nHBV_{short\text{-}term}$ = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.238 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.077 L/kg-d)}}$$

= 618 rounded to 600 ug/L

Reference Dose / Concentration:	0.238 (laboratory animal)
Source of toxicity value:	MDH 2009
Point of Departure:	238 mg/kg-d ($BMDL_{10}$ based on changes in kidney weight calculated by EPA 2005b based on NTP 1990)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	1000
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability, 10 for database deficiencies (to address concerns regarding immunological and neurotoxicity endpoints. Alterations in immune response and in behavior were reported in short-term studies at doses lower than the subchronic POD. These sensitive effects have not been adequately evaluated for this duration. Inhalation studies have also identified neurological effects as a sensitive endpoint.)
Critical effect(s):	Changes in liver and kidney weights (with histological changes at higher doses)
Co-critical effect(s):	Decreased fetal body weight, organ weights (liver and kidney), and placental weight; neurotransmitter level and histological changes in the brain; changes in immune response
Additivity endpoint(s):	Development, Hepatic (liver) system, Immune system, Nervous system, Renal (kidney) system
Secondary effect(s):	Increased heart weight; histological changes in the brain, liver, and kidney; neurological effects; decreased body weight; increased mortality

The subchronic nHBV must be protective of the acute and short-term exposures that occur within the subchronic period and therefore, the subchronic nHBV is set equal to

the Short-term nHBV of 200 ug/L. Additivity Endpoints: Immune system and nervous system.

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = $nHBV_{short\text{-}term}$ = 200 ug/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.079 mg/kg/d) x (0.2) x (1000 ug/mg)}}{\text{(0.043 L/kg-d)}}$$

= 367 rounded to 400 ug/L

Reference Dose / Concentration:	0.079 mg/kg-d (laboratory animal)
Source of toxicity value:	MDH 2009
Point of Departure:	238 mg/kg-d ($BMDL_{10}$ based on changes in kidney weight calculated by EPA 2005b based on NTP 1990)
Human Equivalent Dose Adjustment:	Insufficient data for calculation
Total uncertainty factor:	3000
UF allocation:	10 for interspecies extrapolation, 10 for intraspecies variability, 10 for database deficiencies (to address concerns regarding immunological and neurotoxicity endpoints. Alterations in immune response and in behavior were reported in short-term studies at doses lower than the subchronic POD. These sensitive effects have not been adequately evaluated for this duration. Inhalation studies have also identified neurological effects as a sensitive endpoint.), 3 for use of a subchronic study (an adequate assessment of duration could not be conducted since the shorter-term studies utilized lower dose levels and assessed different endpoints than the longer duration studies.)
Critical effect(s):	Changes in liver and kidney weights (with histological changes at higher doses)
Co-critical effect(s):	Decreased fetal body weight, organ weights (liver and kidney), and placental weight; neurotransmitter level and histological changes in the brain; changes in immune response
Additivity endpoint(s):	Development, Hepatic (liver) system, Immune system, Nervous system, Renal (kidney) system

Secondary effect(s):	Increased heart weight; histological changes in the brain, liver, and kidney; neurological effects; decreased body weight; increased mortality

The chronic nHBV must be protective of acute and short-term exposures that occur within the chronic period and therefore, the chronic nHBV is set equal to the Short-term HBV of 200 ug/L. Additivity Endpoints: Immune system and nervous system.

Cancer Health Based Value (cHBV) = Not applicable

Cancer classification:	Inadequate information to assess the carcinogenic potential in humans (EPA IRIS 2005)
Slope factor:	None
Source of slope factor:	None
Tumor site(s):	None

Volatile: Yes (highly)

Summary of changes since 1993/1994 HRL promulgation:
The short-term, subchronic and chronic HBVs (200 ug/L) are 5-fold lower than the 1993/94 HRL value (1000 ug/L) as the result of : 1) a reassessment of the toxicity; 2) a multi-duration assessment and utilization of higher intake rates; and 3) rounding to one significant figure.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	Yes	Yes	No[4]	Yes
Effects?	Secondary Observations [1]	Yes[2]	Yes[3]	--	Yes[5]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

[1] A 2- to 4-fold increase in the measured amounts of adrenocorticotropic hormone (ACTH) was observed with increasing dose in one short-term study. The biological significance of this effect is uncertain.

[2] Several immunological studies have been conducted. Immunosuppressant effects from toluene exposure have been demonstrated. Statistically significant and dose-related decreases in antibody response were consistently noted in a series of studies by one group of investigators. However, a second group, which conducted a single study, did not find immunosuppression. The two groups of investigators used different mouse strains, different sexes, and utilized different exposure durations. Inhalation studies in laboratory animals also suggest that immunotoxicity may be a sensitive endpoint. The results from the first group of investigators (Hsieh et al) form the basis of the short-term RfD. A database uncertainty factor was incorporated into the derivation of the subchronic and chronic RfD, in part, to address the lack of immunotoxicity data for these durations.

[3] Decreased fetal body weight and organ weights, as well as histological changes in the brain have been reported in several developmental studies at doses more than 20-fold higher than the short-term NOAEL. Histological changes in the brain were reported were also reported in longer-term studies in adults exposed to doses 40-fold higher than the short-term NOAEL. An extended 1 generation study reported behavioral effects in exposed offspring. These effects are identified as short-term co-critical effects. A database UF was incorporated into the derivation of the subchronic and chronic RfDs, in part, to address the need for additional neurotoxicity testing. Data are available on mothers who abused toluene (presumably as an inhalant) during and before pregnancy. Toluene is believed to cause congenital defects in infants under these conditions of high exposure.

[4] Oral multigenerational or reproductive studies have not been conducted. Two subchronic inhalation studies have assessed fertility – one study reported decreased epididymal weight and reduced sperm counts in the highest dose group, the second study reported an increase in testes weight. Neither study reported any histological abnormalities. Other signs of toxicity (e.g., increased kidney weights, decreased body weights, increased mortality) were observed at these high dose levels. A two-generation inhalation study in rats did not report any effects on fertility or histological changes in organs.

[5] Several short-term and subchronic studies have reported changes in brain neurotransmitter levels, histological changes in the brain and mild behavioral changes. However, a dose-response relationship was not always clear. Inhalation studies indicate that the nervous system is a sensitive endpoint. Behavioral effects were identified as co-critical effects for the short-term duration. A database UF was incorporated into the derivation of the subchronic and chronic RfDs, in part, to address the need for additional neurotoxicity testing.

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2009 Health Based Value for Groundwater
Health Risk Assessment Unit, Environmental Health Division
651-201-4899
651-201-5797 TDD

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Chemical Name: Xylenes
CAS: 1330-20-7

Synonyms: o-,m-,p-Xylene; m & p-xylene; m-,p-,o-Xylene; Dimethylbenzene; Dimethylbenzenes; Dimethylbenzene (mixed isomers); except p-xylene, mixed or all isomers; Socal aquatic solvent 3501; Total xylenes; Xylene; Xylene (o-,m-,p-); Xylene (o-, m-, p-isomers); xylenes; Xylenes ; Xylenes (o-, m-, p-isomers); Xylenes (mixed); Xylenes mixed isomers; Xylene (mixed); Xylene (mixed isomers); xylene, mixed or all isomers, except p-; Xylene mixture; Xylene mixture (m-xylene, o-xylene, p-xylene); Xylene mixture (60% m-xylene, 9% o-xylene, 14% p-xylene, 17% ethylbenzene); Xylene, (total); Xylol

Xylenes are a mixture of three isomers: meta-xylene (m-xylene), ortho-xylene (o-xylene), and para-xylene (p-xylene) with the meta-isomer usually being the dominant part of the mixture at 40-70%. The exact composition of the commercial xylene grade depends on the source but a typical mixture will also contain ethylbenzene at 6 - 20% in addition to the three isomers. The environmental fate (transport, partitioning, transformation, and degradation) is expected to be similar for each of the xylene isomers based on the similarities of their physical and chemical properties (Agency for Toxic Substances and Disease Registry 2007). The metabolism of each individual isomer is thought to be similar and the U.S. Environmental Protection Agency, 2003 IRIS Toxicological Review states that, “although differences in the toxicity of the xylene isomers have been detected, no consistent pattern following oral or inhalation exposure has been identified” (U.S. EPA, 2003).

Acute Non-Cancer Health Based Value ($nHBV_{acute}$) = 800 µg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Acute intake rate, L/kg/d)}}$$

$$= \frac{\text{(1.2 mg/kg/d) x (0.2) x (1000 µg/mg)}}{\text{(0.289L/kg-d)}}$$

= 830 rounded to **800 μg/L**

Reference Dose:	1.2 mg/kg-day (laboratory animal)
Source of toxicity value:	MDH 2010 (same as ATSDR Acute MRL 2007)
Point of Departure:	125 mg/kg-day (NOAEL- Dyer et al 1988, p-xylene isomer)
Human Equivalent Dose Adjustment:	NA
Total uncertainty factor:	100
UF allocation:	10 for interspecies variation; 10 for intraspecies variation
Critical effect(s):	Altered visually evoked potentials
Co-critical effect(s):	None
Additivity endpoint(s):	Nervous system
Secondary effect(s):	None

Short-term Non-Cancer Health Based Value ($nHBV_{short\text{-}term}$) = 300 μg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Short-term intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.50 mg/kg/d) x (0.2) x (1000 μg/mg)}}{\text{(0.289 L/kg-d)}}$$

= 346 rounded to **300 μg/L**

Reference Dose:	0.50 mg/kg-day (laboratory animal)
Source of toxicity value:	MDH 2010
Point of Departure:	500 mg/kg-day (NOAEL, NTP 1986; xylene mixture of 60.2% m-xylene, 9.1% o-xylene, 13.6% p-xylene, and 17% ethylbenzene)
Human Equivalent Dose Adjustment:	NA
Total uncertainty factor:	1000
UF allocation:	10 for interspecies variation; 10 for intraspecies variation; 10 for database deficiencies (The database lacked oral multi-generational reproductive as well as adequate ototoxicity and neurotoxicity studies. Inhalation studies have identified neurological effects as a sensitive endpoint.)

Critical effect(s):	Decreased body weight
Co-critical effect(s):	Altered visually evoked potentials, hearing loss as characterized by loss/damage to outer hair cells in cochlea
Additivity endpoint(s):	Nervous system
Secondary effect(s):	Shallow breathing, mortality, decreased thymus and spleen weight, decreased maternal uterine weight, overt maternal toxicity, increased resorptions, and fetal malformations (mainly cleft palate)

Subchronic Non-Cancer Health Based Value ($nHBV_{subchronic}$) = Short-term $nHBV_{short-term}$ = 300 μg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Subchronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.15 mg/kg/d) x (0.2) x (1000 μg/mg)}}{\text{(0.077 L/kg-d)}}$$

= 389 rounded to **400 μg/L**

Reference Dose:	0.15 mg/kg-day (laboratory animal)
Source of toxicity value:	MDH, 2010
Point of Departure:	150 mg/kg-day (NOAEL, Condie et al 1988; xylene mixture of 62.3% m- & p-xylene, 17.6% o-xylene, and 20% ethylbenzene)
Human Equivalent Dose Adjustment:	NA
Total uncertainty factor:	1000
UF allocation:	10 for interspecies variation; 10 for intraspecies variation; 10 for database deficiencies (The database lacked oral multi-generational reproductive as well as adequate ototoxicity and neurotoxicity studies. Inhalation studies have identified neurological effects as a sensitive endpoint.)
Critical effect(s):	Mild nephropathy in females and increased kidney weight in males
Co-critical effect(s):	Decreased body weight, altered visual evoked potential, hearing loss as characterized by loss/damage to outer hair cells in the cochlea

Additivity endpoint(s):	Renal (kidney) system*, Nervous system
Secondary effect(s):	Lethargy, shallow breathing, unsteadiness, tremors, paresis, decreased thymus and spleen weight, decreased body weight, fetal malformations (mainly cleft palate), decreased maternal uterine weight, increased resorptions

The Subchronic nHBV must be protective of the short-term exposures that occur within the subchronic period and therefore, the Subchronic nHBV is set equal to the Short-term nHBV of 300 ug/L. Additivity endpoints: Renal (kidney) system*, Nervous system.

*The short-term and subchronic water concentrations were very similar (346 ug/L – short-term & 389 ug/L – subchronic) so renal effects were included as an additivity endpoint for the subchronic duration even though the subchronic HBV defaulted to the short-term value

Chronic Non-Cancer Health Based Value ($nHBV_{chronic}$) = Short-term $nHBV_{short\text{-}term}$ = 300 μg/L

$$= \frac{\text{(Reference Dose, mg/kg/d) x (Relative Source Contribution) x (Conversion Factor)}}{\text{(Chronic intake rate, L/kg/d)}}$$

$$= \frac{\text{(0.18 mg/kg/d) x (0.2) x (1000 μg/mg)}}{\text{(0.043 L/kg-d)}}$$

= 837 rounded to **800 μg/L**

Reference Dose:	0.18 mg/kg-day (laboratory animal)
Source of toxicity value:	MDH 2010 (same as EPA IRIS 2003)
Point of Departure:	179 mg/kg-day(NOAEL, NTP 1986; xylene mixture of 60% m-xylene, 9.1% o-xylene, 13.6% p-xylene, and 17% ethylbenzene)
Human Equivalent Dose Adjustment:	NA
Total uncertainty factor:	1000
UF allocation:	10 for interspecies variation; 10 for intraspecies variation; 10 for database deficiencies (The database lacked oral multi-generational reproductive as well as adequate ototoxicity and neurotoxicity studies. Inhalation studies have identified neurological effects

	as a sensitive endpoint.)
Critical effect(s):	Decreased body weight
Co-critical effect(s):	Altered visual evoked potential
Additivity endpoint(s):	Renal (kidney) system*, Nervous system
Secondary effect(s):	Hyperactivity, increased kidney weights, minimal nephropathy, hearing loss as characterized by loss/damage to outer hair cells in the cochlea

The Chronic nHBV must be protective of the short-term exposures that occur within the chronic periods and therefore, the Chronic nHBV is set equal to the Short-term nHBV of 300 μg/L. Additivity endpoints: Renal (kidney) system*, Nervous system.

*Renal effects were listed as an additivity endpoint for the chronic duration because the chronic HBV must be protective of effects that occur during the subchronic duration. Even though the chronic duration HBV defaulted to the short-term value, renal effects were added as an additivity endpoint for the subchronic duration. The short-term and subchronic water concentrations were very similar (346 μg/L – short-term & 389 μg/L – subchronic) so renal effects were included as an additivity endpoint for the subchronic duration even though the subchronic HBV also defaulted to the short-term value.

Cancer Health Based Value (cHBV) = Not Applicable

Cancer classification:	None
Slope factor:	NA
Source of slope factor:	NA
Tumor site(s):	NA

Volatile: Yes (highly)

Summary of Guidance Value History:
The short-term, subchronic, and chronic HBV is 33 times lower than the 1993/94 HRL (10,000 ug/L) as the result of: 1) a 4-fold fold lower, revised RfD, 2) utilizing more recent intake rates which incorporate higher intake rates during early life, and 3) rounding to one significant digit.

Summary of toxicity testing for health effects identified in the Health Standards Statute:

	Endocrine	Immunotoxicity	Development	Reproductive	Neurotoxicity
Tested?	No	Yes	Yes	Yes	Yes
Effects?	No	Yes[1]	Yes[2]	Yes[3]	Yes[4]

Note: Even if testing for a specific health effect was not conducted for this chemical, information about that effect might be available from studies conducted for other purposes. Most chemicals have been subject to multiple studies in which researchers identify a dose where no effects were observed, and the lowest dose that caused one or more effects. A toxicity value based on the effect observed at the lowest dose across all available studies is considered protective of all other effects that occur at higher doses.

Comments on extent of testing or effects:

1. Decreased spleen and thymus and spleen weights were measured following oral exposure at a dose two times higher than the short-term critical study LOAEL (1000 mg/kg-day) and are identified as secondary effects for the short-term and subchronic durations.
2. Developmental testing found effects of malformations including cleft palate, decreased fetal body weight and increased fetal death at doses two times higher than the LOAEL in the short-term critical study. Developmental effects were listed as a secondary effect for the short-term duration.
3. Reproductive effects including increased resorptions and decreased uterine weight following oral exposure at doses two times higher than the short-term critical study LOAEL (1000 mg/kg-day) and eight times higher than the acute critical study LOAEL (250 mg/kg-day).
4. Neurological effects of transient hyperactivity were seen at oral doses during the chronic duration that were three times higher than the critical acute LOAEL (250 mg/kg-day) which was based on altered evoked visual potentials. Transient signs of nervous system depression were observed in mice at oral doses that were six time higher than the acute LOAEL (250 mg/kg-day) and two times higher than the subchronic critical study LOAEL (750 mg/kg-day). Neurological effects were listed as critical, co-critical, and secondary effects. Neurotoxicity has been identified as the most sensitive endpoint following inhalation exposure.

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