Background

• In January, 2017 EPA published updated Human Health Benchmarks for Pesticides (HHBPs) in drinking water to reflect the latest scientific information and methodologies.

• HHBPs are levels of certain food use pesticides in water at or below which adverse health effects are not anticipated from one-day or lifetime exposures.

• HHBPs are intended to be used for informational purposes by states, tribes, water systems and the public to help interpret monitoring data for pesticides for which there are no drinking water standards or health advisories.

• HHBPs are updated on a semi-regular basis to reflect toxicity assessments provided by the Office of Pesticide Programs (OPP) and Exposure Factors Handbook (2011).
Current Update

• This update includes the following changes:
  • Updated publicly available toxicity information developed by OPP,
  • Inclusion of Food Quality Protection Act (FQPA) safety factors in the calculations, and
  • Updated exposure factors for body weight and drinking water intake to represent the most current science.
<table>
<thead>
<tr>
<th>Common Name and Reference Document</th>
<th>Acute or One Day PAD (mg/kg/day)</th>
<th>0.005 Acute or One Day HHBBPs (ppb) Children</th>
<th>Chronic or Lifetime PAD (mg/kg/day)</th>
<th>0.03 Chronic or Lifetime HHBBPs (ppb)</th>
<th>Chronic HHBBP Sensitive Lifestage/Population</th>
<th>General Population</th>
<th>Cancer Quantification (Q1) Values (CSF) (mg/kg/per day)</th>
<th>Carcinogenic HHBBP (E-6 to E-4) (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,2,4-Triazole</td>
<td>0.03</td>
<td>200</td>
<td>Children</td>
<td>0.005</td>
<td>Chronic HHBBP Sensitive Lifestage/Population</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2,4-DB DMA</td>
<td>0.6</td>
<td>20000</td>
<td>Females 13-49 years</td>
<td>0.03</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2,4-DBA</td>
<td>0.6</td>
<td>20000</td>
<td>Females 13-49 years</td>
<td>0.03</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2,4-DP-p Salts &amp; Esters</td>
<td>0.05</td>
<td>300</td>
<td>Children</td>
<td>0.036</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>2,6-Dichlorobenzamide (BAM)</td>
<td>0.1</td>
<td>700</td>
<td>Children</td>
<td>0.0045</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>4-Chlorophenoxycetic acid</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>1.32</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>ADBAC</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>0.44</td>
<td>General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>
Calculation of Benchmarks

• Benchmarks are derived using toxicity values (i.e., RfDs) and/or cancer slope factors and exposure assumptions similar to methods used to develop drinking water health advisories (HA).

\[
\text{Acute or one-day HHBP (for children) (ppb) = } \frac{a\text{RfD (mg/kg/day) } \times 1000 (\mu g/mg)}{0.15 (L/kg-day) \text{ DWI-BW ratio}}
\]

\[
\text{Acute or one-day HHBP (females 13-49 years) (ppb) = } \frac{a\text{RfD (mg/kg/day) } \times 69 \text{ (kg) BW } \times 1000 (\mu g/mg)}{2.5 \text{ (L/day) DWI}}
\]

\[
\text{Chronic non-cancer HHBP (general population) (ppb) = } \frac{c\text{RfD (mg/kg/day) } \times 80 \text{ (kg) BW } \times 1000 (\mu g/mg) \times 0.2 \text{ RSC}}{2.5 \text{ (L/day) DWI}}
\]

\[
\text{Chronic non-cancer HHBP (females 13-49 years) (ppb) = } \frac{c\text{RfD (mg/kg/day) } \times 69 \text{ (kg) BW } \times 1000 (\mu g/mg) \times 0.2 \text{ RSC}}{2.5 \text{ (L/day) DWI}}
\]

\[
\text{Drinking Water Unit Risk (\mu g/L or ppb) = } \frac{\text{CSF (mg/kg/day) } \times 2.5 \text{ (L/day) (adult DWI))}}{80 \text{ (kg) (Adult BW) } \times 1000 (\mu g/mg)}
\]

From the drinking water unit risk, the following $10^{-6}$ to $10^{-4}$ cancer risk specific levels in water are determined.

\[
10^{-6} \text{ or } 10^{-4} \text{ Risk Level in Drinking Water (ppb) = } \frac{10^{-6} \text{ or } 10^{-4}}{\text{Drinking Water Unit Risk (ppb)}}
\]
Summary

Attached is a summary table of the acute and chronic reference doses which have been established by the Office of Pesticide Programs (OPP) for dietary risk assessments.

The table includes those chemicals that have been reviewed by the Health Effects Division of OPP from July 1987 through August 2015. For many of the chemicals, when appropriate, a separate acute reference dose has been established for two distinct sub-populations: the general population and females age 13 through 49. A similar division for the chronic reference dose has been made, when appropriate, for a limited number of chemicals.

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Exposure</th>
<th>NOAEL</th>
<th>UF</th>
<th>RfD</th>
<th>PAI</th>
<th>LOAEL</th>
<th>Results</th>
<th>Species</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiodicarb</td>
<td>Acute Dietary, General Population</td>
<td>Not Est.</td>
<td>300</td>
<td>0.033</td>
<td>0.011</td>
<td>10.00</td>
<td>Decreased maternal body weight gain.</td>
<td>Rat</td>
<td>Developmental Toxicity</td>
</tr>
<tr>
<td>Thiodicarb</td>
<td>Acute Dietary, Females 13-49</td>
<td>Not Est.</td>
<td>300</td>
<td>0.033</td>
<td>0.011</td>
<td>10.00</td>
<td>Decreased fetal body weight and increased number of litters and fetuses with developmental variations.</td>
<td>Rat</td>
<td>Developmental Toxicity</td>
</tr>
<tr>
<td>Thiodicarb</td>
<td>Chronic Dietary, General Population</td>
<td>3.00</td>
<td>100</td>
<td>0.03</td>
<td>0.011</td>
<td>12.00</td>
<td>Decreased RBC ChE and increased incidence of extramedullary hematopoiesis.</td>
<td>Rat</td>
<td>Chronic/Carcinogenicity</td>
</tr>
<tr>
<td>Thiophanate-methyl</td>
<td>Acute Dietary, General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>An appropriate endpoint attributable to a single dose was not identified.</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Thiophanate-methyl</td>
<td>Acute Dietary, Females 13-49</td>
<td>20.00</td>
<td>100</td>
<td>0.20</td>
<td>0.2</td>
<td>40.00</td>
<td>Increased incidences of supernumerary ribs.</td>
<td>Rabbit</td>
<td>Developmental Toxicity</td>
</tr>
<tr>
<td>Thiophanate-methyl</td>
<td>Chronic Dietary, General Population</td>
<td>8.00</td>
<td>300</td>
<td>0.0267</td>
<td>0.0267</td>
<td>40.00</td>
<td>Decreases in body weight, body weight gain and alterations in thyroid hormones, thyroid weights and histopathological lesions in the thyroids.</td>
<td>Dog</td>
<td>Chronic</td>
</tr>
</tbody>
</table>
Application of the Food Quality Protection Act Safety Factor (FQPA)

• This update also includes use of RfDs that include Food Quality Protection Act or FQPA Safety Factors.

• For pesticide registrations under FIFRA, EPA derives acute or chronic population adjusted doses (PADs) using an FQPA Safety Factor mandated by the FQPA taking into consideration potential pre and/or post natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.

• In the majority of instances, the PAD and the RfD are the same. It is only in those few instances when the FQPA Safety Factor is attributed to residual uncertainty with regard to exposure or pre/post natal toxicity that the RfD and PAD differ.

• More recently, FQPA safety factors can account for uncertainties in the overall completeness of the toxicity database, extrapolation from subchronic to a chronic study duration, and LOAEL to NOAEL extrapolation. For this reason, HHBP values were calculated using the PADs.
The Agency has determined that the data provided no indication of increased susceptibility of rats or rabbits to in utero or postnatal exposure to thiodicarb. In the prenatal developmental toxicity studies in rats and rabbits, effects in the fetuses were observed only at or above treatment levels that resulted in evidence of maternal toxicity. In the two-generation reproduction toxicity study, although the effects in the offspring were observed at a calculated lower dose (calculated NOEL = 1.75 mg/kg/day) than in the

There are, however, data gaps for acute and subchronic neurotoxicity studies in rats. These studies are considered data gaps because thiodicarb breaks down to methomyl, which has exhibited neurotoxic signs in two species (dogs and rabbits) by two
The RfD for thiodicarb was calculated to be 0.03 mg/kg/day from a chronic rat toxicity study with a NOEL of 3.3 mg/kg/day for males and 4.5 mg/kg/day for females. The RfD was based on an increased incidence of extramedullary hemopoiesis in males and decreased RBC cholinesterase in females at the LOEL. An uncertainty factor of 100 was used for deriving the RfD and includes 10x for inter-species extrapolation and 10x for intra-species variation. An FQPA safety factor of 3x (due to data gaps) was applied to derive an FQPA adjusted RfD of 0.01 mg/kg/day. Exposure must be less than 100% of the FQPA adjusted RfD to be considered below EPA’s level of concern.

Acute Dietary (1 day) Females 13 Years and Older

The endpoint selected for this risk assessment is the developmental LOEL equal to 10 mg/kg/day, based on decreased fetal body weight and an increase in the number of litters and fetuses with developmental variations. This endpoint is applicable only for the females 13 years and older subgroup. For acute dietary risk assessment for thiodicarb alone, a MOE of 1000 is required. This MOE includes the conventional MOE of 100 for inter- and intra-species variation, 3x for FQPA, and another 3x for the use of a LOEL, instead of the NOEL, in the critical study. The FQPA Safety Factor (3x) is required because of data gaps (acute and subchronic neurotoxicity studies).
### Summary

Attached is a summary table of the acute and chronic reference doses which have been established by the Office of Pesticide Programs (OPP) for dietary risk assessments.

The table includes those chemicals that have been reviewed by the Health Effects Division of OPP from July 1997 through August 2015. For many of the chemicals, when appropriate, a separate acute reference dose has been established for two distinct subpopulations: the general population and females 13 through 49. A similar division for the chronic reference dose has been made, when appropriate, for a limited number of chemicals.

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Exposure</th>
<th>NOAEL</th>
<th>UF</th>
<th>RfD</th>
<th>POPAD</th>
<th>LOAEL</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiocarb</td>
<td>Acute Dietary, General Population</td>
<td>Not Est.</td>
<td>300</td>
<td>0.033</td>
<td>0.011</td>
<td>10.0</td>
<td>Decreased maternal body weight gain.</td>
</tr>
<tr>
<td>Thiocarb</td>
<td>Acute Dietary, Females 13-49</td>
<td>Not Est.</td>
<td>300</td>
<td>0.033</td>
<td>0.011</td>
<td>10.0</td>
<td>Decreased fetal body weight and increased number of litters and fetuses with developmental variations.</td>
</tr>
<tr>
<td>Thiocarb</td>
<td>Chronic Dietary, General Population</td>
<td>3.00</td>
<td>100</td>
<td>0.03</td>
<td>0.011</td>
<td>12.0</td>
<td>Decreased RBC ChE and increased incidence of extramedullary hematopoiesis.</td>
</tr>
<tr>
<td>Thiocarb</td>
<td>Acute Dietary, General Population</td>
<td>--</td>
<td>--</td>
<td>--</td>
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<td>--</td>
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</tr>
</tbody>
</table>
Updated Exposure Factors for Adults

Body Weight

• **Updated weight: 80 kilograms**
  • Based on 1999 to 2006 National Health and Nutrition Examination Survey (NHANES) data (EPA ORD’s 2011 *Exposure Factors Handbook*).
  • Represents the mean weight for adults.

• **Previous weight: 70 kilograms**
  • Based on 1988 to 1994 NHANES III database and a 1989 study conducted by the National Cancer Institute.
  • Represented the mean weight for adults.

Drinking Water Intake

• **Updated rate: 2.5 liters per day**
  • Based on 2003 to 2006 NHANES data (EPA’s 2011 *Exposure Factors Handbook*).
  • Represents the per capita estimate of combined direct and indirect community water ingestion at the 90th percentile for adults.

• **Previous rate: 2 liters per day**
  • Based on a 1994 to 1996 USDA survey.
  • Represented the per capita community water ingestion rate at the 86th percentile for adults surveyed.
Updated Exposure Factors for Women and Children

• For children and females of reproductive age, the following exposure assumptions were used:
  • The body weight for females of reproductive age (13-49 years) was updated from 66 kg to 69 kg based on NHANES data from 1999 to 2006.
  • For children, a normalized ratio of drinking water ingestion to body weight (DWI/ BW) of 0.15 L/kg/day was calculated using data for infants (birth to <12 months) and this represents the 90th percentile values of the consumers-only estimates of direct and indirect water ingestion based on 1994-1998 CSFII (Continuing Survey of Food Intakes by Individuals).
Summary of Update

• 394 pesticides listed
• Updated body weight and drinking water intake
• Significant figures correspond to the number of significant figures in the toxicity value used to derive the benchmark
• Benchmarks for 3 pesticides removed (d-Allethrin, S-Bioallethrin, and Bioallethrin)
Summary of Changes

• 41 previously listed pesticides have updated toxicity values
  • 33 have updated RfD values but did not apply an FQPA factor > 1
  • 8 have updated RfD values and apply FQPA factors > 1

• 28 previously listed pesticides did not have new toxicity values but had previously unincorporated FQPA factors > 1 that were included in this update

• 38 pesticides that were not previously on the table were added based on new toxicity values
  • 8 have FQPA factors > 1
# Summary of Changes in Toxicity Values*

<table>
<thead>
<tr>
<th>Type of Benchmark</th>
<th>Direction of Change in Toxicity Value</th>
<th>Pesticides with Change</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute</td>
<td>Increase (Less Stringent)</td>
<td>2,6-Dichlorobenzamide (BAM), Acetochlor, Bromoxynil, Bromoxynil octanoate, Chlorfenapyr, Dimethenamid, Dimethenamid-P, Fenzaquin, Fosthiazate, Furfural, Indaziflam, Indoxacarb, Mancozeb, Metaldehyde, Pinoxaden, Topramezone</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Decrease (More Stringent)</td>
<td>Bifenthrin, Carbendazim (MBC), Chlorpyrifos methyl, Clodinafop-propargyl, Cypermethrin, Deltamethrin, Dinocap, Fenitrothion, Fenpropadín, Hexaconazole, Imazaquin, Methidathion, Mevinphos, Norflurazon, Pendimethalin, Phorate, Phosmet, Pirimiphos-methyl, Prallethrin, Sulfosate (Glyphosate-trimesium), Tefluthrin, Thiodicarb, Tribufos, Trichlorfon, Triphenyltin hydroxide (TPTH), Vinclozolin, Zeta-Cypermethrin, Ziram</td>
<td>31</td>
</tr>
<tr>
<td>Chronic</td>
<td>Increase (Less Stringent)</td>
<td>Aminocyclopyrachlor, Chlorfenapyr, Chlorosulfuron, Clethodim, Cyromazine, Dinofuran, Flupirimidol, Fosthiazate, Mancozeb, Mesotrione, Metaldehyde, Naphthalene Acetates, Oxytetracycline hydrochloride, Pendimethalin, Pinoxaden, Sulfentrazone</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Decrease (More Stringent)</td>
<td>Asulam, Carbendazim (MBC), Chlorpyrifos methyl, Clodinafop-propargyl, Dinocap, Fenitrothion, Imazaquin, Imazapic, Methidathion, Mevinphos, PCNB (Quintozone), Pendimethalin, Phorate, Phosmet, Pirimiphos-methyl, Sulfosate (Glyphosate-trimesium), Terrazole, Thiodicarb, Tribufos, Trichlorfon, Triphenyltin hydroxide (TPTH), Vinclozolin, Ziram</td>
<td>26</td>
</tr>
</tbody>
</table>

*Reference Dose/Population Adjusted Dose (RfD/PAD)
Additional Information

• EPA pesticide risk assessments available on the web at http://www.epa.gov/pesticides


• Contact Jamie Strong at strong.jamie@epa.gov