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Health Effects Support Document for Metribuzin

External Review Draft

Health Effects Support Document for Metribuzin

EXTERNAL REVIEW DRAFT

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FOREWORD

The Safe Drinking Water Act (SDWA), as amended in 1996, requires the Administrator of the Environmental Protection Agency to establish a list of contaminants to aid the agency in regulatory priority setting for the drinking water program. In addition, SDWA requires EPA to make regulatory determinations for no fewer than five contaminants by August 2001. The criteria used to determine whether or not to regulate a chemical on the CCL are the following:

The contaminant may have an adverse effect on the health of persons.

The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern.

In the sole judgment of the administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

The Agency's finding for the criteria are used in making a determination to regulate a contaminant. The Agency may determine that there is no need for regulation when a contaminant fails to meet one of the criteria. The decision not to regulate is considered a final agency action and is subject to judicial review.

This document provides the health effects basis for the preliminary regulatory determination for metribuzin. In arriving at the preliminary regulatory determination, data on toxicokinetics, human exposure, acute and chronic toxicity to animals and humans, epidemiology, and mechanisms of toxicity were evaluated. In order to avoid wasteful duplication of effort, information from the following risk assessments by the EPA and other government agencies were used in development of this document.

U.S. EPA. 1998a. U.S. Environmental Protection Agency. Registration Eligibility Decision (RED): Metribuzin. Office of Prevention, Pesticides, and Toxic Substances. June 1997.

U.S. EPA. 1998b. U.S. Environmental Protection Agency. R.E.D. Facts: Metribuzin. Office of Prevention, Pesticides, and Toxic Substances. June 1997.

U.S. EPA. 1988. U.S. Environmental Protection Agency. Health advisories for 50 pesticides. Office of Drinking Water. August 1988.

U.S. EPA. 1993. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS): Metribuzin. Cincinnati, OH. December 1, 1993.

Information from the published risk assessments was supplemented with information from recent studies of metribuzin identified by literature searches conducted in 1999 and 2000 and the primary references for key studies.

Generally a Reference Dose (RfD) is provided as the assessment of long-term toxic effects other than carcinogenicity. RfD determination assumes that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in terms of milligrams per kilogram per day (mg/kg-day). In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The carcinogenicity assessment for metribuzin includes a formal hazard identification. Hazard identification is a weight-of-evidence judgment of the likelihood that the agent is a human carcinogen via the oral route and the conditions under which the carcinogenic effects may be expressed.

Guidelines that were used in the development of this assessment may include the following: the *Guidelines for Carcinogen Risk Assessment* (U.S. EPA,1986a), *Guidelines for the Health Risk Assessment of Chemical Mixtures* (U.S. EPA, 1986b), *Guidelines for Mutagenicity Risk Assessment* (U.S. EPA, 1986c), *Guidelines for Developmental Toxicity Risk Assessment* (U.S. EPA, 1991), *Proposed Guidelines for Carcinogen Risk Assessment* (1996a), *Guidelines for Reproductive Toxicity Risk Assessment* (U.S. EPA, 1996b), and *Guidelines for Neurotoxicity Risk Assessment* (U.S. EPA, 1998a); *Recommendations for and Documentation of Biological Values for Use in Risk Assessment* (U.S. EPA, 1988); and Health Effects Testing Guidelines (OPPTS series 870, 1996 drafts; U.S. EPA 40 CFR Part 798, 1997); *Peer Review and Peer Involvement at the U.S. Environmental Protection Agency* (U.S. EPA, 1994c); *Use of the Benchmark Dose Approach in Health Risk Assessment* (U.S. EPA, 1995b); *Science Policy Council Handbook: Peer Review* (U.S. EPA, 1998b, 2000a); Memorandum from EPA Administrator, Carol Browner, dated March 21, 1995, Policy for Risk Characterization; *Science Policy Council Handbook: Risk Characterization* (U.S. EPA, 2000b)

The chapter on occurrence and exposure to metribuzin through potable water was developed by the Office of Ground Water and Drinking Water. It is based primarily on unregulated contaminant monitoring (UCM) data collected under SDWA. The UCM data are supplemented with ambient water data as well as information on production, use, and discharge.

ACKNOWLEDGMENTS

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1.0 EXECUTIVE SUMMARY

The U.S. Environmental Protection Agency (EPA) has prepared this Health Effects Support Document for Metribuzin to support a preliminary determination regarding whether to regulate metribuzin with a National Primary Drinking Water Regulation (NPDWR). The available data on occurrence, exposure, and other risk considerations suggest that, because metribuzin does not occur in public water systems at frequencies and levels of public health concern, regulating metribuzin will not present a meaningful opportunity to reduce health risk. EPA will present a determination and further analysis in the Federal Register Notice covering the CCL proposals.

Metribuzin (Chemical Abstracts Services Registry Number 21087-64-9) is a synthetic organic compound used as a selective triazinone herbicide. It is a white crystalline solid, is soluble in water up to 1,200 ppm (1.2 g/L), and has a sulfurous odor. Metribuzin is released into the environment primarily during agricultural spraying operations and is moderately absorbed on soils with high clay or organic content. It may be released into surface and ground waters during runoff events in agricultural regions. Metribuzin is listed as a Toxic Release Inventory (TRI) chemical, with air emissions constituting the majority of on-site releases.

Human exposure to metribuzin occurs through inhalation and ingestion, usually in agricultural settings. Although it is applied to food crops to discourage the growth of broadleaf weeds and grasses, metribuzin has not been detected in any food samples tested. Occupational exposure to metribuzin includes agricultural workers, sprayers, and handlers. General population exposures are thought to be minimal. There are no reports of accidental human exposures to metribuzin.

There is little information on the adverse health effects of metribuzin exposure to humans. Hazard characterization has therefore been accomplished in animal toxicity studies. Acute studies in animals indicate that metribuzin exhibits a low order of toxicity, as indicated by high LD_{50} values. Acute exposure studies also indicate that metribuzin does not possess ocular or dermal irritation properties. Subchronic studies suggest that metribuzin could cause adverse effects in body weight gain, organ weight, and hematological parameters. Specifically, studies in Wistar rats indicate that liver and thyroid weights were increased and body weight gain was decreased. In rats, chronic effects may include changes in body weight gain, liver enzyme activities and histopathological changes. In addition, increases in corneal neovascularization and discolored zones in the liver, and enlarged adrenal and thyroid glands, have been observed in rats. At high doses, chronic metribuzin exposure has been observed to cause significant increases in mortality, liver dysfunction, and thyroid weight in Beagle dogs. Developmental studies in rats and rabbits indicate that effects to the fetus only occur subsequent to maternal toxicity. Similarly, in reproductive studies, both parents and pups experienced decreased body weight and exaggerated liver cell growth.

Drinking water monitoring of metribuzin is conducted under the Unregulated Contaminant Monitoring (UCM) program. Metribuzin was not among the contaminants monitored in Round 1 of the UCM program; metribuzin monitoring began in Round 2. A cross-section analysis of 20 states participating in Round 2 of the UCM program indicate that the frequency of detection of metribuzin in public water systems (PWSs) is low. The 20-state cross-section analysis indicates that 0.007% of

PWSs detected metribuzin at levels above the Minimum Reporting Level (MRL). The percentage of the population served by PWSs reporting metribuzin detections is 0.0003%. National extrapolation of this data indicates that 5 PWSs nationally would contain detectable levels of metribuzin, and that 1000 people would be exposed. However, no drinking water concentrations of metribuzin in the cross-section analysis were greater than the Health Reference Level (HRL) or half the HRL. Using more conservative estimates of occurrence from all states reporting Round 2 monitoring data, including states with biased data, 0.28% of the nation's PWSs (approximately 182 systems and 3.4 million people served) are affected by metribuzin concentrations > MRL, while no PWSs are affected by concentrations > ½ HRL or > HRL.

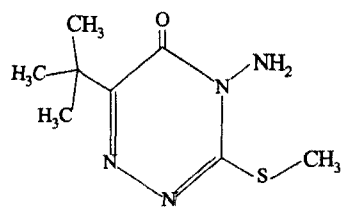
In accordance with current cancer guidelines, metribuzin is classified as a Class D carcinogen due to inadequate carcinogenicity data in humans and animals. Chronic exposure studies in rats and mice were negative for the induction of tumors by metribuzin. Based on a 2-year feeding study in rats, the oral Reference Dose (RfD) was determined to be 0.013 mg/kg-day.

2.0 IDENTITY: PHYSICAL AND CHEMICAL PROPERTIES

Metribuzin is a white crystalline solid with a melting point of 126 °C. Pure metribuzin is soluble in water up to 1,200 ppm (1.2 g/L). It is also soluble in dimethylformamide at 1,780, cyclohexanone at 1,000, chloroform at 850, acetone at 820, ethylacetate at 470, methanol at 450, dichloromethane at 333, benzene at 220, n-butanol at 150, ethanol at 190, toluene at 120, xylene at 90 and n-hexane at 2 g/kg at 20 °C. Metribuzin has a slight sulfurous odor. It is reported to have a vapor pressure of between 5 and 10 mm Hg at 20°C and a density of 1.28 between 4 and 20°C (U.S. EPA, 1998a; HSDB, 2000).

Common Name:	Metribuzin
Chemical Name:	4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one
Chemical Family:	Triazinone
CAS Registry Number:	21087-64-9
Molecular Weight:	214.28
Empirical Formula:	$C_8H_{14}N_4OS$

Metribuzin Structural Formula:



Metribuzin has several trade names and synonyms. These names and synonyms are listed below in alphabetical order (RTECS, 2000; HSDB, 2000; U.S. EPA, 1998a).

4-Amino-6-tert-butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one
4-Amino-6-tert-butyl-3-(methylthio)-as-triazin-S(4H)-one
4-Amino-6-tert-butyl-3-(methylthio)-as-triazin-5(4H)-one
4-Amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one
4-Amino-6-tert-butyl-3-(methylthio)- 1,2,4-triazin-5-one
Bay 61597, Bayer 94337, Bay DIC 1468, Bayer 6159H, Bayer 6443H
DIC 1468, NTN 70
Lexone, Lexone DF, Lexone 4L
Metribuzine, Preview
Sencor, Sencor 4, Sencoral, Sencor DF, Sencorer, Sencorex , Sengoral
Zenkor

3.0 USES AND ENVIRONMENTAL FATE

3.1 Production and Use

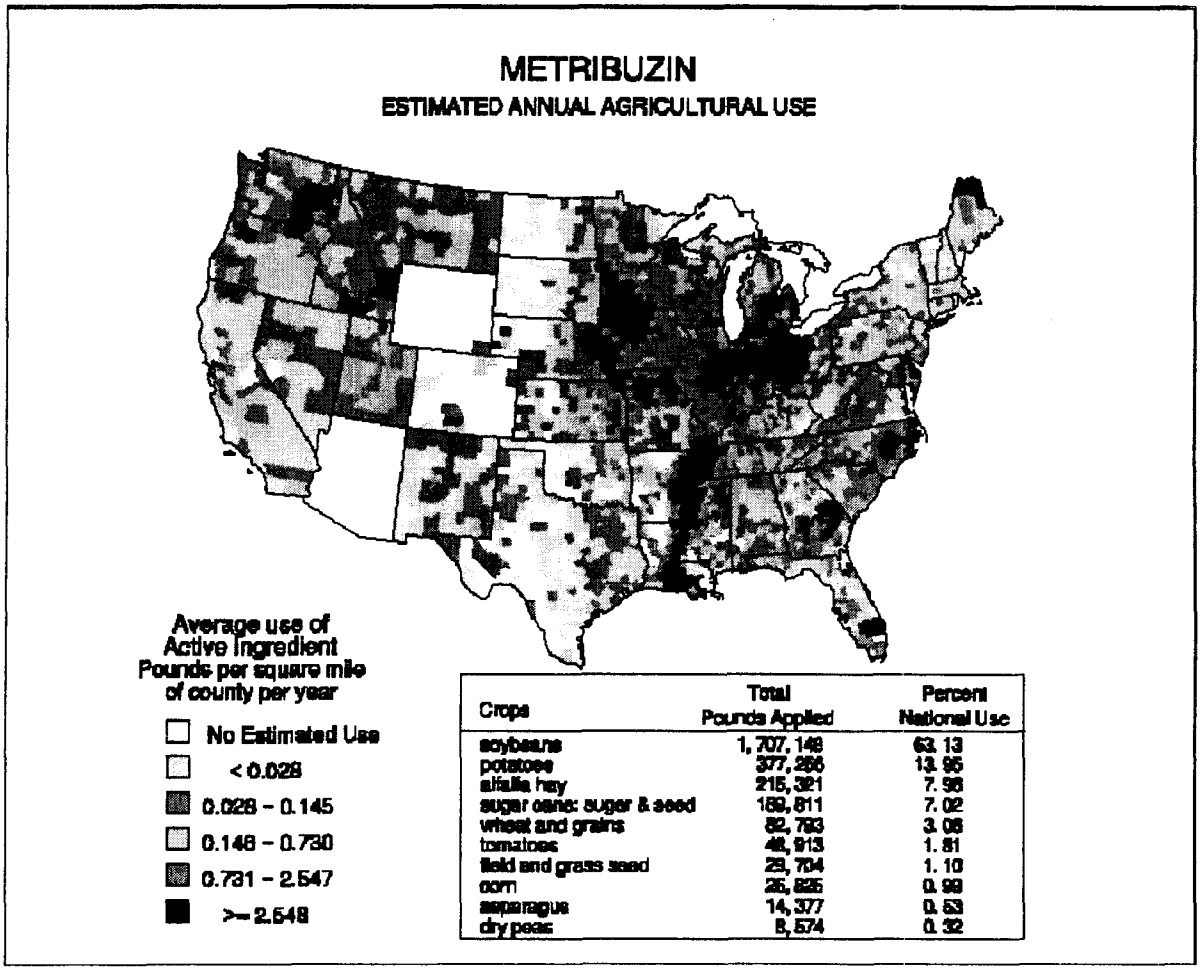
Metribuzin is a synthetic organic compound (SOC). It is a selective triazinone herbicide used primarily to discourage growth of broadleaf weeds and annual grasses among vegetable crops and turf grass. Metribuzin accomplishes this by inhibiting electron transport in photosynthesis (EXTOXNET, 1998; U.S. EPA, 1998a). Common uses include application to soybeans, potatoes, alfalfa, sugarcane, barley, and tomatoes (Larson et al., 1999; U.S. EPA, 1998a).

Recent national estimates of agricultural use for metribuzin are available. Using its own proprietary data, data from the United States Department of Agriculture (USDA) and the National Center for Food and Agricultural Policy (NCFAP), the U.S. EPA (1998a) estimated U.S. average annual use for the years 1990-94 at approximately 2.8 million pounds of active ingredient (a.i.) with approximately 8.5 million acres treated. The United States Geological Survey (USGS) estimated approximately 2.7 million pounds of active ingredient used for the year 1992, with roughly 8.4 million acres treated (USGS, 2000a). These estimates were derived using state-level data sets on pesticide use rates available from NCFAP combined with county-level data on harvested crop acreage from the Census of Agriculture (CA) (Thelin and Gianessi, 2000).

Figure 3-1 shows the geographic distribution of estimated average annual metribuzin use in the United States for 1992. A breakdown of use by crop is also included. Non-agricultural uses are not reflected here and any sharp spatial differences in use within a county are not well represented (USGS, 1998a). Existing data suggest that non-agricultural use of metribuzin is minimal (U.S. EPA, 1998a).

Metribuzin use patterns have been documented by the USDA as well. USDA Cropping Practices Surveys (CPS) for field crops (1964-1995) merged with the Farm Costs and Returns Survey (FCRS) in 1996 to form the Agricultural Resources Management Study (ARMS). As was the case with the CPSs, the ARMS is conducted in major producing states and provides information on metribuzin use on particular field crops (corn, soybeans, cotton, winter wheat, spring and durum wheat, and fall potatoes). Farm operators are surveyed for crop practice information on a field-by-field basis (USDA, 1997; USDA, 2000). Table 3-1 shows the amount of metribuzin used annually and the number of acres treated. Metribuzin use appears to be modestly declining over the ten-year period.

Figure 3-1. Estimated Annual Agricultural Use for Metribuzin (1992).



Crops	Total Pounds Applied	Percent National Use
soybeans	1,707,148	63.13
potatoes	377,266	13.95
alfalfa hay	215,321	7.96
sugar cane: sugar & seed	189,811	7.02
wheat and grains	82,783	3.06
tomatoes	48,913	1.81
field and grass seed	29,704	1.10
corn	26,825	0.99
asparagus	14,377	0.53
dry peas	8,574	0.32

USGS, 1998b

Table 3-1. Metribuzin Use, 1990-1999.

Year	Pounds of Active Ingredient (x 1000)	Acres Treated (x 1000)
1999	1,214	4,542*
1998	1,261	6,432
1997	2,207	8,646
1996	1,785	6,547
1995	1,498	5,892
1994	1,773	5,811
1993	2,003	6,437
1992	1,975	6,705
1991	2,537	7,706
1990	2,959	8,924

Data for the years 1990-1995, USDA, 1997
Data for the years 1996-1999, USDA, 2000
**average figure based on available data*

3.2 Environmental Release

Metribuzin is also listed as a toxic release inventory (TRI) chemical. In 1986, the Emergency Planning and Community Right-to-Know Act (EPCRA) established the Toxic Release Inventory (TRI) of hazardous chemicals. Created under the Superfund Amendments and Reauthorization Act (SARA) of 1986, EPCRA is also sometimes known as SARA Title III. The EPCRA mandates that larger facilities publicly report when TRI chemicals are released into the environment. This public reporting is required for facilities with more than 10 full-time employees that annually manufacture or produce more than 25,000 pounds, or use more than 10,000 pounds, of TRI chemical (U.S. EPA, 1996; U.S. EPA, 2000d).

Under these conditions, facilities are required to report the pounds per year of metribuzin released into the environment both on- and off-site. The on-site quantity is subdivided into air emissions, surface water discharges, underground injections, and releases to land (see Table 3-2). For metribuzin, air emissions constitute most of the on-site releases; these emissions decrease throughout the period of record. A sharp decrease is evident between the 1996 and 1997 reporting years. In contrast, over the period for which data are available (1995-1998), surface water discharges generally increase. Again, the trend is exaggerated between the reporting years

Table 3-2. Environmental Releases (in pounds) for Metribuzin in the United States, 1995-1998.

Year	On-Site Releases				Off-Site Releases	Total On- & Off-site Releases
	Air Emissions	Surface Water Discharges	Underground Injection	Releases to Land		
1998	339	26	0	0	255	620
1997	359	24	0	0	0	383
1996	1,012	5	0	0	0	1,017
1995	1,936	9	0	0	0	1,945

U.S. EPA, 2000b

1996 and 1997. Whether these abrupt shifts reflect actual increases in surface water discharges and decreases in air emissions is unclear. Interpretation is confounded by the relatively short period of record. These TRI data for metribuzin were reported from three states and one territory (IA, MO, NB, Puerto Rico; U.S. EPA, 2000b).

Although the TRI data can be useful in giving a general idea of release trends, it is far from exhaustive and has significant limitations. For example, only industries that meet TRI criteria (at least 10 full-time employees, and manufacture and process quantities exceeding 25,000 lbs/yr, or use of more than 10,000 lbs/yr) are required to report releases. These reporting criteria do not account for releases from smaller industries. Threshold manufacturing and processing quantities also changed from 1988-1990 (dropping from 75,000 lbs/yr in 1988 to 50,000 lbs/yr in 1989 to its current 25,000 lbs/yr in 1990) creating possibly misleading data trends. Also, the TRI data is meant to reflect releases and should not be used to estimate general exposure to a chemical (U.S. EPA, 2000c; U.S. EPA, 2000a).

In summary, metribuzin is used as an herbicide on crops and has limited non-agricultural use. Applications are primarily targeted to soybeans, potatoes, alfalfa, and sugar cane, and the geographic distribution of use largely reflects the distribution of these crops across the United States (Figure 3-1). Estimated annual use appears to be modestly declining in the last decade (Table 3-1). Metribuzin is also a TRI chemical. Industrial releases have been reported since 1995 in three states and one U.S. territory.

3.3 Environmental Fate

Metribuzin is released into the environment primarily during agricultural spraying operations. It is moderately adsorbed on soils with high clay or organic content, as reflected by the organic carbon partition coefficient (K_{oc} = 95) (HSDB, 2000). Adsorption decreases with increasing soil pH since metribuzin is adsorbed via a hydrogen-bonding mechanism. Although little leaching occurs in soils with a high organic content, metribuzin is readily leached in sandy soils. The soil half-life ranges from 14-60 days.

Based on its low vapor pressure, metribuzin should exist in the vapor and particulate phases at ambient temperature (HSDB, 2000). In the vapor phase, metribuzin is degraded by reaction with photochemically formed hydroxyl radicals with a half-life of approximately 11 hours (HSDB, 2000). In the particulate phase, metribuzin is removed from the atmosphere by dry deposition. In addition, metribuzin has been detected in rainwater, indicating that it can be removed from air by wet deposition (HSDB, 2000).

The primary fate process for metribuzin in soil is microbial degradation (HSDB, 2000). The rate of degradation is increased by the activity of soil microorganisms, higher temperatures, and aerobic conditions. Metribuzin is degraded to carbon dioxide in soil. Metabolites observed in plants, such as the 3,5-diketo and deaminated diketo metribuzin, have been found in soil (HSDB, 2000). Loss from soil surfaces by photodecomposition and volatilization are not expected (HSDB, 2000).

In the aquatic environment, volatilization from water and bioconcentration in fish are not anticipated to be relevant (HSDB, 2000). No data are available for the biodegradation of metribuzin in water.

4.0 EXPOSURE FROM DRINKING WATER

4.1 Occurrence and Monitoring Data of Ambient Water

To understand the presence of a chemical in the environment, an examination of ambient occurrence is useful. In a drinking water context, ambient water is source water existing in surface waters and aquifers before treatment. The most comprehensive and nationally consistent data describing ambient water quality in the United States are being produced through the United States Geological Survey's (USGS) National Ambient Water Quality Assessment (NAWQA) program. NAWQA, however, is a relatively young program and complete national data are not yet available from their entire array of sites across the nation.

4.1.1 Data Sources and Methods

The USGS instituted the NAWQA program in 1991 to examine water quality status and trends in the United States. NAWQA is designed and implemented in such a manner to allow consistency and comparison between representative study basins located around the country, facilitating interpretation of natural and anthropogenic factors affecting water quality (Leahy and Thompson, 1994).

The NAWQA program consists of 59 significant watersheds and aquifers referred to as "study units." The study units represent approximately two-thirds of the overall water usage in the United States and a similar proportion of the population served by public water systems. Approximately one half of the nation's land area is represented (Leahy and Thompson, 1994).

To facilitate management and make the program cost-effective, approximately one-third of the study units at a time engage in intensive assessment for a period of 3 to 5 years. This is followed by a period of less intensive research and monitoring that lasts between 5 and 7 years. This way all 59 study units rotate through intensive assessment over a ten-year period (Leahy and Thompson, 1994). The first round of intensive monitoring (1991-96) targeted 20 watersheds which were slanted toward agricultural basins. A national synthesis of results from these study units focusing on pesticides and nutrients has been compiled and analyzed (Kolpin et al., 1998; Larson et al., 1999; USGS, 1999).

Metribuzin is an analyte for both surface and ground water NAWQA studies. Two of the first round study units, the Central Nebraska Basins and the White River Basin in Indiana, are located in the corn belt where metribuzin is heavily used (see Figure 3-1). The Method Detection Limit (MDL) for metribuzin is 0.004 µg/L (Kolpin et al., 1998), substantively lower than most drinking water monitoring reporting levels. Additional information on analytical methods used in the NAWQA study units, including method detection limits, are described by Gilliom and others (in press).

Data are also available for metribuzin occurrence in ground water and surface water for key corn belt states. The majority of these data are the result of USGS regional water quality

investigations with a focus on near-surface aquifers and surface waters. Additionally, EPA's Pesticides in Ground Water Database (PGWD) provides a large data set on pesticide occurrence in ground water that spans a period of 20 years and contains data from 68,824 sites. It is a compilation of numerous national, regional, state, and local studies and therefore the data are a mix of the results of a variety of study designs, sampling techniques, and reporting limits. However, the size and temporal scope of the data set make it a valuable resource. Details regarding sampling and analytical methods for the USGS studies and the PGWD report are described in the respective reports.

4.1.2 Results

NAWQA National Synthesis

Detection frequencies and concentrations of metribuzin in ambient surface and ground water are low, especially in ground water (Table 4-1). Most herbicides monitored in the first round of the NAWQA program were detected in the greatest concentrations and frequencies in surface water compared to ground water. Surface waters show the highest maximum concentration of metribuzin at 0.5 µg/L, well below the Health Reference Level (HRL) of 91 µg/L. The Health Reference Level is a preliminary estimated health effect level used for the present analysis.

Frequencies and concentrations of metribuzin in streams in agricultural settings are greater than those in urban settings, with integrator sites (a combination of agricultural and urban) having the highest occurrence (Table 4-1). Larson and others (1999) found that for 50 stream sites monitored over a 1-year period, one site had a detection frequency of > 50% of all samples (detections were reported for metribuzin concentrations ≥ 0.01 µg/L). Ninety percent of sites, however, had detection frequencies of less than 20% of all samples. The annual mean frequency of metribuzin detection was less than 15% in all land-use settings at all concentrations (calculated as the average of the 12 monthly detection frequencies from each site; Larson et al., 1999).

While occurrence in ground water is considerably lower than in surface water, detection in > 1% of ground water samples at concentrations ≥ 0.05 µg/L makes metribuzin one of the 21 most commonly detected pesticides in the first round of intensive NAWQA monitoring (the 21 are detected at concentrations ≥ 0.05 µg/L in more than 10% of stream samples or more than 1% of ground water samples). Metribuzin exceeded the ground water criteria partly because its high water solubility and low soil adsorption potential allow it to leach into ground water (USGS, 2000b; U.S. EPA, 1998b; EXTOXNET, 1998). Also, the herbicide ranks among the top 200 agricultural pesticides in use (USGS, 1999).

Table 4-1. Metribuzin Detections and Concentrations in Streams and Ground Water.

	Detection frequency (% samples ≥ MDL*)		Concentration percentiles (all samples µg/L)		
	% ≥ 0.004 µg/L	% ≥ 0.01 µg/L	median	95th	maximum
streams					
urban	6.73%	5.50%	nd**	0.011	0.100
integrator	14.29%	9.39%	nd	0.020	0.130
agricultural	13.70%	8.20%	nd	0.016	0.330
all sites	13.82%	9.94%	nd	0.026	0.530
ground water					
shallow urban	1.66%	0.33%	nd	nd	0.043
shallow agricultural	3.46%	2.81%	nd	nd	0.300
major aquifers	0.75%	0.32%	nd	nd	0.045
all sites	1.95%	1.36%	nd	nd	0.300

USGS, 2000b
** MDL (Method Detection Limit) for metribuzin in water studies: 0.004 µg/L*
***not detected in concentration greater than MDL*

Herbicides often demonstrate detection frequencies in streams that correlate with patterns of use (USGS, 2000b). Patterns of pesticide use often do not correlate with detection frequency in ground water, probably because of the variable effect of local hydrogeologic conditions (depth and type of aquifer, soil conditions) on pesticides in ground water (USGS, 2000b). Metribuzin, however, is one of six pesticides that, for shallow ground water, demonstrate a statistically significant correlation between detection frequency and intensity of use (Kolpin et al., 1998). Metribuzin detection frequencies are higher in shallow ground water in agricultural areas when compared with shallow ground water in urban areas (Table 4-1). This is most likely a result of metribuzin's primary use as an agricultural pesticide (U.S. EPA, 1998a). Metribuzin is detected most frequently in shallow ground water from land-use categories containing wheat, wheat and alfalfa, corn and soybeans, and corn and alfalfa as major crops or crop-groups (Table 4-2).

Table 4-2. Metribuzin Detections in Shallow Ground Water from Various Land-Use Settings.

Land-use settings*	Detection frequency ≥0.004 µg/L	Detection frequency ≥0.010 µg/L
All	3.1%	nr**
Corn and soybeans > 20%	6.6%	≤ 10%
Corn and alfalfa > 20%	2.1%	0 - 2%
Corn > 50%	0.0%	0 - 2%
Peanuts > 50%	1.6%	< 5%
Wheat and small grains > 50%	9.3%	< 10%
Wheat and small grains and alfalfa > 20%	6.2%	≤ 5%
Alfalfa > 50%	0.0%	0 - 2%
Pasture > 90%	0.0%	0 - 2%
Orchards or vineyards > 50%	0.0%	0 - 2%
Urban	1.8%	0 - 2%

after Kolpin et al., 1998

**evaluated as crop-groups occupying a percent of the total land*

***not reported*

Water Quality Investigations from the Corn Belt

USGS regional water quality investigations and other state and national studies are summarized below to provide ambient data in states where metribuzin use is high (see Figure 3-1). Midwest ground water concentrations and detection frequencies were low during the years 1991-1994 (Table 4-3). The highest detected ground water concentration, 25.1 µg/L, is found in the national Pesticides in Ground Water Database, which draws only a portion of its data from Midwestern states. This concentration is still well below the Health Reference Level (HRL) of 91 µg/L.

Maximum concentrations of metribuzin in surface waters of the Mississippi River and major tributaries for all years, peaking at < 0.1µg/L, were considerably lower than the HRL. Although all 9 sampling sites in the Mississippi River and major tributaries had a least one detection of metribuzin (100% of sites) from April 1991 to March 1992, the percentage of samples with detections was 40%.

Table 4-3. Metribuzin Occurrence in Midwest Surface and Ground Water.

	Ground water ≥ MRL		Surface water ≥ MRL		Max. conc. µg/L
	% sites	% samples	% sites	% samples	
USGS					
Midwest Near-Surface Aquifers (1991)[1]	1.3%	1.0%			0.57
Midwest Near-Surface Aquifers (1992-94)[2]	nr	1.4%			0.22
Miss. River and Major Tributaries (1991)[3]			54%	nr	0.08
Miss. River and Major Tributaries (1991-92)[4]			100%	40%	0.03
Midwest Reservoirs (1992)[5]			12%	6.5%	nr
Pesticides in Ground Water Database (1971-91)[6]	4.3%	nr			25.1

[1] *Kolpin et al., 1994*
[2] *Kolpin et al., 1996*
[3] *Periera and Hostettler, 1993 (cited in Larson et al., 1997)*
[4] *Goolsby and Battaglin, 1993 (cited in Larson et al., 1997)*
[5] *Goolsby et al., 1993 (cited in Larson et al., 1997)*
[6] *U.S. EPA, 1992 (cited in Barbash and Resek, 1996); data are national results including some Midwestern states*
- The Health Reference Level (HRL) used for metribuzin is 91 µg/L. This is a draft value for working review only.
- Minimum Reporting Levels (MRL) vary by study.
- nd = results below the respective reporting level
- nr = "not reported"

4.2 Occurrence and Monitoring Data in Drinking Water

The Safe Drinking Water Act (SDWA), as amended in 1986, required Public Water Systems (PWSs) to monitor for specified "unregulated" contaminants on a five-year cycle and to report the monitoring results to the states. Unregulated contaminants do not have an established or proposed National Primary Drinking Water Regulation (NPDWR), but they are contaminants that were formally listed and were required for monitoring under federal regulations. The intent was to gather scientific information on the occurrence of these contaminants to enable a decision as to whether or not regulations were needed. All non-purchased community water systems (CWSs) and non-purchased non-transient non-community water systems (NTNCWSs), with greater than 150 service connections, were required to conduct this unregulated contaminant monitoring. Smaller systems were not required to conduct this monitoring under federal regulations, but were required to be available for monitoring if the state decided such monitoring was necessary. Many states collected data from smaller systems. Additional contaminants were added to the Unregulated Contaminant Monitoring (UCM) program in 1991 (56 FR 3526) for required monitoring that began in 1993 (57 FR 31776).

Metribuzin has been monitored under the SDWA Unregulated Contaminant Monitoring (UCM) program since 1993 (57 FR 31776). Monitoring ceased for small PWSs under a direct final rule published January 8, 1999 (64 FR 1494), and ended for large PWSs with promulgation of the new Unregulated Contaminant Monitoring Regulation (UCMR) issued September 17, 1999 (64 FR 50556) and effective January 1, 2001. At the time the UCMR lists were developed, the Agency concluded there were adequate monitoring data for a regulatory determination. This obviated the need for continued monitoring under the new UCMR list.

4.2.1 Data Sources, Data Quality, and Analytical Methods

Currently, there is no complete national record of unregulated or regulated contaminants in drinking water from PWSs collected under SDWA. Many states have submitted unregulated contaminant PWS monitoring data to EPA databases, but there are issues of data quality, completeness, and representativeness. Nonetheless, a significant amount of state data are available for UCM contaminants that can provide estimates of national occurrence.

The National Contaminant Occurrence Database (NCOD) is an interface to the actual occurrence data stored in the Safe Drinking Water Information System/Federal version (SDWIS/FED) and can be queried to provide a summary of the data in SDWIS/FED for a particular contaminant. The drinking water occurrence data for metribuzin presented here were derived from monitoring data available in the SDWIS/FED database.

The data in this report have been reviewed, edited, and filtered to meet various data quality objectives for the purposes of this analysis. Hence, not all data from a particular source were used, only data meeting the quality objectives described below were included. The sources of these data, their quality and national aggregation, and the analytical methods used to estimate a given contaminant's national occurrence (from these data) are discussed in this section (for further details see U.S. EPA, 2001a,b).

UCM Rounds 1 and 2

The 1987 UCM contaminants include 34 volatile organic compounds (VOCs) (52 FR 25720). Metribuzin, a synthetic organic compound (SOC), was *not* among these contaminants. The UCM (1987) contaminants were first monitored coincident with the Phase I regulated contaminants, during the 1988-1992 period. This period is often referred to as "Round 1" monitoring. The monitoring data collected by the PWSs were reported to the states (as primacy agents), but there was no protocol in place to report these data to U.S EPA. These data from Round 1 were collected by U.S EPA from many states over time and put into a database called the Unregulated Contaminant Information System, or URCIS.

The 1993 UCM contaminants include 13 SOCs and 1 inorganic contaminant (IOC) (56 FR 3526). Monitoring for the UCM (1993) contaminants began coincident with the Phase II/V regulated contaminants from 1993 through 1998. This is often referred to as "Round 2" monitoring. The UCM (1987) contaminants were also included in the Round 2 monitoring. As

with other monitoring data, PWSs reported these results to the states. EPA, during the past several years, requested that the states submit these historic data which is now stored in the SDWIS/FED database.

Monitoring and data collection for metribuzin, a UCM (1993) contaminant, began in Round 2. Therefore, the following discussion regarding data quality screening, data management, and analytical methods focuses on SDWIS/FED. Discussion of the URCIS database is included where relevant, but it is worth noting that the various quality screening, data management, and analytical processes were nearly identical for the two databases. For further details on the two monitoring periods as well as the databases, see U.S. EPA (2001a and 2001b).

Developing a Nationally Representative Perspective

The Round 2 data contain contaminant occurrence data from a total of 35 primacy entities (including 34 states and data for some tribal systems). However, data from some states are incomplete and biased. Furthermore, the national representativeness of the data is problematic because the data were not collected in a systematic or random statistical framework. These state data could be heavily skewed to low-occurrence or high-occurrence settings. Hence, the state data were evaluated based on pollution-potential indicators and the spatial/hydrologic diversity of the nation. This evaluation enabled the construction of a cross-section from the available state data sets that provides a reasonable representation of national occurrence.

A national cross-section from these state Round 2 contaminant databases was established using the approach developed for the EPA report *A Review of Contaminant Occurrence in Public Water Systems* (U.S. EPA, 1999). This approach was developed to support occurrence analyses for EPA's Chemical Monitoring Reform (CMR) evaluation. It was supported by peer reviewers and stakeholders. The approach cannot provide a "statistically representative" sample because the original monitoring data were not collected or reported in an appropriate fashion. However, the resultant "national cross-section" of states should provide a clear indication of the central tendency of the national data. The remainder of this section provides a summary description of how the national cross-section for the SDWIS/FED (Round 2) database was developed. The details of the approach are presented in other documents (U.S. EPA, 2001a,b); readers are referred to these for more specific information.

Cross-Section Development

As a first step in developing the cross-section, the state data contained in the SDWIS/FED database (containing the Round 2 monitoring results) were evaluated for completeness and quality. Some state data in SDWIS/FED were unusable for a variety of reasons. Some states reported only detections, or their data had incorrect units. Datasets only including detections are obviously biased. Other problems included substantially incomplete data sets without all PWSs reporting (U.S. EPA, 2001a Sections II and III).

The balance of the states remaining after the data quality screening were then examined to establish a national cross-section. This step was based on evaluating the states' pollution potential and geographic coverage in relation to all states. Pollution potential is considered to ensure a selection of states that represent the range of likely contaminant occurrence, and a balance with regard to likely high and low occurrence. Geographic consideration is included so that the wide range of climatic and hydrogeologic conditions across the United States are represented, again balancing the varied conditions that affect transport and fate of contaminants, as well as conditions that affect naturally occurring contaminants (U.S. EPA, 2001b Sections III.A. and III.B.).

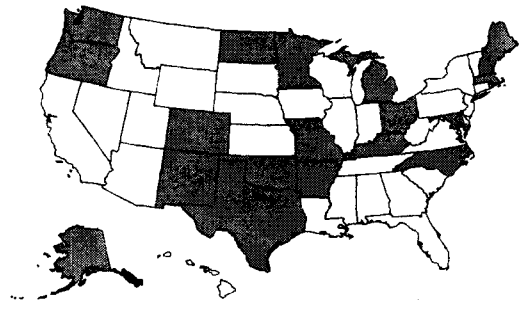
The cross-section states were selected to represent a variety of pollution potential conditions. Two primary pollution potential indicators were used. The first factor selected indicates pollution potential from manufacturing/population density and serves as an indicator of the potential for VOC contamination within a state. Agriculture was selected as the second pollution potential indicator because the majority of SOCs of concern are pesticides (U.S. EPA, 2001b Section III.A.). The 50 individual states were ranked from highest to lowest based on the pollution potential indicator data. For example, the state with the highest ranking for pollution potential from manufacturing received a ranking of 1 for this factor and the state with the lowest value was ranked as number 50. States were ranked for their agricultural chemical use status in a similar fashion.

The states' pollution potential rankings for each factor were subdivided into four quartiles (from highest to lowest pollution potential). The cross-section states were chosen from all quartiles for both pollution potential factors to ensure representation, for example, from: states with high agrichemical pollution potential rankings and high manufacturing pollution potential rankings; states with high agrichemical pollution potential rankings and low manufacturing pollution potential rankings; states with low agrichemical pollution potential rankings and high manufacturing pollution potential rankings; and states with low agrichemical pollution potential rankings and low manufacturing pollution potential rankings (U.S. EPA, 2001b Section III.B.). In addition, some secondary pollution potential indicators were considered to further ensure that the cross-section states included the spectrum of pollution potential conditions (high to low). The cross-section was then reviewed for geographic coverage throughout all sectors of the United States.

The data quality screening, pollution potential rankings, and geographic coverage analysis established a national cross-section of 20 Round 2 (SDWIS/FED) states. The cross-section states provide good representation of the nation's varied climatic and hydrogeologic regimes and the breadth of pollution potential for the contaminant groups (Figure 4-1).

Figure 4-1. Geographic Distribution of Cross-Section States for Round 2 (SDWIS/FED).

Round 2 (SDWIS/FED)	
Alaska	New Hampshire
Arkansas	New Mexico
Colorado	North Carolina
Kentucky	North Dakota
Maine	Ohio
Maryland	Oklahoma
Massachusetts	Oregon
Michigan	Rhode Island
Minnesota	Texas
Missouri	Washington



Cross-Section Evaluation

To evaluate and validate the method for creating the national cross-sections, the method was used to create smaller state subsets from the 24-state, Round 1 (URCIS) cross-section and aggregations. Again, states were chosen to achieve a balance from the quartiles describing pollution potential and a balanced geographic distribution, to incrementally build subset cross-sections of various sizes. For example, the Round 1 cross-section was tested with subsets of 4, 8 (the first 4 state subset plus 4 more states), and 13 (8 state subset plus 5) states. Two additional cross-sections were included in the analysis for comparison: a cross-section composed of 16 biased states eliminated from the 24 state cross-section for data quality reasons and a cross-section composed of all 40 Round 1 states (U.S. EPA, 2001b Section III.B.1).

These Round 1 incremental cross-sections were then used to evaluate occurrence for an array of both high- and low-occurrence contaminants. The comparative results illustrate several points. The results are quite stable and consistent for the 8-, 13-, and 24-state cross-sections. They are much less so for the 4-state, 16-state (biased), and 40-state (all Round 1 states) cross-sections. The 4-state cross-section is too small to provide balance both geographically and with pollution potential, a finding that concurs with past work (U.S. EPA, 1999). The CMR analysis suggested that a minimum of 6-7 states was needed to provide balance both geographically and with pollution potential, and the CMR report used 8 states out of the available data for its nationally representative cross-section (U.S. EPA, 1999). The 16-state and 40-state cross-sections, both including biased states, provided occurrence results that were unstable and inconsistent for a variety of reasons associated with their data quality problems (U.S. EPA, 2001b Section III.B.1).

The 8-, 13-, and 24-state cross-sections provide very comparable results, are consistent, and are usable as national cross-sections to provide estimates of contaminant occurrence.

Including greater data from more states improves the national representation and the confidence in the results, as long as the states are balanced in terms of pollution potential and spatial coverage. The 20-state cross-section provides the best, nationally representative cross-section for the Round 2 data.

4.2.2 Data Management and Analysis

The cross-section analyses focused on occurrence at the water system level; i.e., the summary data presented discuss the percentage of public water *systems* with detections, not the percentage of *samples* with detections. By normalizing the analytical data to the system level, skewness inherent in the sample data is avoided. System level analysis was used since a PWS with a known contaminant problem usually has to sample more frequently than a PWS that has never detected the contaminant. The results of a simple computation of the percentage of samples with detections (or other statistics) can be skewed by the more frequent sampling results reported by the contaminated site. The system level of analysis is conservative. For example, a system need only have a single sample with an analytical result greater than the Minimum Reporting Limit (MRL), i.e., a detection, to be counted as a system with a result "greater than the MRL."

Also, the data used in the analyses were limited to only those data with confirmed water source and sampling type information. Only standard SDWA compliance samples were used; "special" samples, or "investigation" samples (investigating a contaminant problem that would bias results), or samples of unknown type were not used in the analyses. Various quality control and review checks were performed, including follow-up questions to the states providing the data. Many of the most intractable data quality problems encountered occurred with older data. These problematic data were, in some cases, simply eliminated from the analysis. For example, when the number of data with problems were insignificant relative to the total number of observations they were dropped from the analysis (For further details see Cadmus, 2000).

As indicated in Figure 4-1, Massachusetts is included in the 20-state, Round 2 national cross-section. Noteworthy for SOCs like metribuzin, however, Massachusetts' SOC data were problematic. Massachusetts reported Round 2 sample results for SOCs from only 56 PWSs, while reporting VOC results from over 400 different PWSs. Massachusetts SOC data also contained an atypically high percentage of systems with analytical detections when compared to all other states. Through communications with Massachusetts data management staff it was learned that the state's SOC data were incomplete and that the SDWIS/FED record for Massachusetts SOC data was also incomplete. For instance, the SDWIS/FED Round 2 data for Massachusetts indicates 14.3% of systems reported detections of metribuzin. The cross-section state with the next highest detection frequency reported only 0.2% of systems with detections. In contrast, Massachusetts' data characteristics and quantities for IOCs and VOCs were reasonable and comparable with other states' results. Therefore, Massachusetts was included in the group of 20 SDWIS/FED Round 2 cross-section states with usable data for IOCs and VOCs, but its metribuzin (SOC) data were omitted from Round 2 cross-section occurrence analyses and summaries presented in this report.

Occurrence Analysis

To evaluate national contaminant occurrence, a two-stage analytical approach has been developed. The first stage of analysis provides a straightforward, conservative, broad evaluation of occurrence of the CCL preliminary regulatory determination priority contaminants as described above. These descriptive statistics are summarized here. Based on the findings of the Stage 1 Analysis, EPA will determine whether more intensive statistical evaluations, the Stage 2 Analysis, may be warranted to generate national probability estimates of contaminant occurrence and exposure for priority contaminants. (For details on this two stage analytical approach see Cadmus, 2000.)

The summary descriptive statistics presented in Table 4-4 for metribuzin are a result of the Stage 1 analysis and include data from Round 2 (SDWIS/FED, 1993-1997) cross-section states (minus Massachusetts). Included are the total number of samples, the percent of samples with detections, the 99th percentile concentration of all samples, the 99th percentile concentration of samples with detections, and the median concentration of samples with detections. The percentages of PWSs and population served indicate the proportion of PWSs whose analytical results showed a detection(s) of the contaminant (simple detection, > MRL) at any time during the monitoring period; or a detection(s) greater than one-half the Health Reference Level (HRL); or a detection(s) greater than the Health Reference Level. The Health Reference Level, 91 µg/L, is a preliminary estimated health effect level used for this analysis.

The HRL was derived from the RfD (developed in Chapter 8 of this document) as a preliminary estimated health effect level as follows:

$$HRL = \frac{RfD \times Body\ Weight}{Drinking\ Water\ Intake} \times Relative\ Source\ Contribution$$

$$HRL = \frac{0.013\ mg/kg \times 70\ kg}{2L} \times 20\%$$

$$HRL = 0.091\ mg/L \text{ or } 91\ \mu g/L$$

The 99th percentile concentration is used here as a summary statistic to indicate the upper bound of occurrence values because maximum values can be extreme values (outliers) that sometimes result from sampling or reporting error. The 99th percentile concentration is presented for both the samples with only detections and all of the samples because the value for the 99th percentile concentration of all samples is below the Minimum Reporting Level (MRL) (denoted by "<" in Table 4-4). For the same reason, summary statistics such as the 95th percentile

Table 4-4. Summary Occurrence Statistics for Metribuzin.

Frequency Factors	20 State Cross-Section[1] (Round 2)	All Reporting States[2] (Round 2)	National System and Population Numbers[3]	
Total Number of Samples	34,507	42,856	–	
Percent of Samples with Detections	0.003%	0.23%	–	
99th Percentile Concentration (all samples)	< (Non -detect)	< (Non -detect)	–	
Health Reference Level	91 µg/L	91 µg/L	–	
Minimum Reporting Level (MRL)	Variable[4]	Variable[4]	–	
99th Percentile Concentration of Detections	0.10 µg/L	3.0 µg/L	–	
Median Concentration of Detections	0.10 µg/L	1.0 µg/L	–	
Total Number of PWSs	13,512	15,333	65,030	
Number of GW PWSs	11,833	13,311	59,440	
Number of SW PWSs	1,679	2,022	5,590	
Total Population	50,633,068	62,397,416	213,008,182	
Populations of GW PWSs	14,886,153	16,255,818	85,681,696	
Populations of SW PWSs	35,746,915	46,141,598	127,326,486	
Occurrence by System			National Extrapolation[5]	
% PWSs with detections (>MRL)	0.007%	0.28%	5	182
Range	0-0.17%	0-14.29%	N/A	N/A
GW PWSs with detections	0.008%	0.14%	5	83
SW PWSs with detections	0.00%	1.24%	0	69
%PWSs > ½ Health Reference Level (HRL)	0.00%	0.00%	0	0
Range	0-0.00%	0-0.00%	N/A	N/A
GW PWSs > ½ Health Reference Level	0.00%	0.00%	0	0
SW PWSs > ½ Health Reference Level	0.00%	0.00%	0	0
% PWSs > Health Reference Level	0.00%	0.00%	0	0
Range	0-0.00%	0-0.00%	N/A	N/A
GW PWSs > Health Reference Level	0.00%	0.00%	0	0
SW PWSs > Health Reference Level	0.00%	0.00%	0	0
Occurrence by Population Served				
% PWS Populations Served with detections	0.0003%	1.61%	1,000	3,429,000
Range	0-0.01%	0-14.92%	N/A	N/A
GW PWS Population with detections	0.00%	0.24%	1,000	206,000
SW PWS Populations with detections	0.00%	2.09%	0	2,661,000
% PWS Population Served > ½ Health Reference Level	0.00%	0.00%	0	0
Range	0-0.00%	0-0.00%	N/A	N/A
GW PWS Population > ½ Health Reference Level	0.00%	0.00%	0	0
SW PWS Population > ½ Health Reference Level	0.00%	0.00%	0	0
% PWS Population Served > Health Reference Level	0.00%	0.00%	0	0
Range	0-0.00%	0-0.00%	N/A	N/A
GW PWS Population > Health Reference Level	0.00%	0.00%	0	0
SW PWS Population > Health Reference Level	0.00%	0.00%	0	0

[1] Summary Results based on data from 20-State Cross-Section (minus Massachusetts), from SDWIS/FED, UCM (1993) Round 2.

[2] Summary Results based on data from all reporting states from SDWIS/FED, UCM (1993) Round 2.

[3] Total PWS and population numbers are from EPA March 2000 Water Industry Baseline Handbook (U.S. EPA, 2000e).

[4] See text for discussion.

[5] National extrapolations are from the 20-State cross-section data (left) and all Round 2 states reporting data (right) using the Baseline Handbook system and population numbers.

- PWS = Public Water Systems; GW = Ground Water; SW = Surface Water; MRL = Minimum Reporting Level (for laboratory analyses); HRL = Health Reference Level, an estimated health effect level used for preliminary assessment for this review; N/A = Not Applicable.

- The Health Reference Level (HRL) used for metribuzin is 91 µg/L. This is a draft value for working review only.

- Total Number of Samples = the total number of analytical records for metribuzin.

- 99th Percentile Concentration = the concentration value of the 99th percentile of either all analytical results or just the detections (in µg/L)- Median Concentration of Detections = the median analytical value of all the detections (analytical results greater than the MRL) (in µg/L)

- Total Number of PWSs = the total number of public water systems with records for metribuzin

- Total Population Served = the total population served by public water systems with records for metribuzin

- % PWS with detections, % PWS > ½ Health Reference Level, % PWS > Health Reference Level = percent of the total number of public water systems with at least one analytical result that exceeded the MRL, ½ Health Reference Level, Health Reference Level, respectively

- % PWS Population Served with detections, % PWS Population Served >½ Health Reference Level, % PWS Population Served > Health Reference Level = percent of the total population served by PWSs with at least one analytical result exceeding the MRL, ½ Health Reference Level, or the Health Reference Level, respectively

concentration of all samples or the median (or mean) concentration of all samples are omitted because these also are all "<" values. This is the case because only 0.003% of all samples recorded detections of metribuzin in Round 2.

As a simplifying assumption, a value of one-half the MRL is often used as an estimate of the concentration of a contaminant in samples/systems whose results are less than the MRL. For a contaminant with relatively low occurrence, such as metribuzin in drinking water occurrence databases, the median or mean value of occurrence using this assumption would be half the MRL (0.5 × MRL). However, for these occurrence data this is not straightforward. For Round 2, states have reported a wide range of values for the MRLs. This is in part related to state data management differences as well as real differences in analytical methods, laboratories, and other factors.

The situation can cause confusion when examining descriptive statistics for occurrence. For example, most Round 2 states reported non-detections as zeros resulting in a modal MRL value of zero. By definition the MRL cannot be zero. This is an artifact of state data management systems. Because a simple meaningful summary statistic is not available to describe the various reported MRLs, and to avoid confusion, MRLs are not reported in the summary table (Table 4-4).

In Table 4-4, national occurrence is estimated by extrapolating the summary statistics for the 20-state cross-section (minus Massachusetts) to national numbers for systems, and population served by systems, from the *Water Industry Baseline Handbook, Second Edition* (U.S. EPA, 2000e). From the handbook, the total number of community water systems (CWSs) plus non-transient, non-community water systems (NTNCWSs) is 65,030, and the total population served by CWSs plus NTNCWSs is 213,008,182 persons (see Table 4-4). To arrive at the national occurrence estimate for the cross-section, the national estimate for PWSs (or population served by PWSs) is simply multiplied by the percentage for the given summary statistic [i.e., the national estimate for the total number of PWSs with detections (5) is the product of the percentage of PWSs with detections (0.007%) and the national estimate for the total number of PWSs (65,030)].

Included in Table 4-4, in addition to the results from the cross-section data, are results and national extrapolations from all Round 2 reporting states. The data from the biased states are included because of metribuzin's very low occurrence in drinking water samples in all states. For contaminants with very low occurrence, such as metribuzin where very few states have detections, any occurrence becomes more important, relatively. For such contaminants, the cross-section process can easily miss a state with occurrence that becomes more important. This is the case with metribuzin.

Extrapolating only from the cross-section states, metribuzin's very low occurrence clearly underestimates national occurrence. For example, while data from biased states like Massachusetts exaggerate occurrence because of incomplete reporting, the detections are real and need to be accounted for because extrapolations from the cross-section states do not predict

enough detections in the biased states. Therefore, results from all reporting Round 2 states, including the biased states, are also used here to extrapolate a national estimate. Using the biased states' data should provide conservative estimates of national occurrence for metribuzin.

As exemplified by the cross-section extrapolations for metribuzin, national extrapolations of these Stage 1 analytical results can be problematic, especially for contaminants with very low occurrence, because the State data used for the cross-section are not a strict statistical sample. For this reason, the nationally extrapolated estimates of occurrence based on Stage 1 results are not presented in the CCL Federal Register Notice. The presentation in the Federal Register Notice of only the actual results of the cross-section analysis maintains a straight-forward presentation, and the integrity of the data, for stakeholder review. The nationally extrapolated Stage 1 occurrence values are presented here, however, to provide additional perspective. A more rigorous statistical modeling effort, the Stage 2 analysis, could be conducted on the cross-section data (Cadmus, 2001). The Stage 2 results would be more statistically robust and more suitable to national extrapolation. This approach would provide a probability estimate and would also allow for better quantification of estimation error.

Additional Drinking Water Data from the Corn Belt

To augment the SDWA drinking water data analysis described above, and to provide additional coverage of the corn belt states where metribuzin use is highest (Figure 3-1), independent analyses of finished drinking water data from the states of Iowa, Illinois, Indiana, and Ohio are reviewed below. The Iowa analysis examined SDWA compliance monitoring data from surface and ground water PWSs for the years 1988-1995 (Hallberg et al., 1996). Illinois and Indiana compliance monitoring data for surface and ground water PWSs were evaluated. The data were mostly for the years from 1993 to 1997, though some earlier data were also analyzed (after U.S. EPA, 1999). These state data sets were available from an independent review of contaminant monitoring in drinking water (U.S. EPA, 1999). Finally, the Ohio Round 2 data analyzed with the 20-state cross-section are examined independently for comparison with the other supplemental data sets from corn belt states.

Additional reviews of national and state drinking water monitoring results are included for further perspective on corn belt occurrence of metribuzin. The Iowa State-Wide Rural Well-Water Survey was conducted in 1988-1989 to assess pesticide occurrence in rural private wells (Kross et al., 1990). The National Pesticide Survey (NPS) provides extensive national monitoring data for drinking water, including data from Midwestern states, for the years 1988-1990 (U.S. EPA, 1990). Hallberg (1989) reviewed special contaminant occurrence studies of raw surface water supplies in Illinois (1985-1987), and both raw and finished drinking water from surface water in Iowa (1986). Data sources, data quality, and analytical methods for these analyses are described in the respective reports.

4.2.3 Results

Occurrence Estimates

As noted, the extrapolation from cross-section states underestimates national metribuzin occurrence, and the resulting percentages of PWSs with detections are very low (Table 4-4). The cross-section shows approximately 0.007% of PWSs (about 5 PWSs nationally) experienced detections of metribuzin above the MRL, affecting less than 0.0003% of the population served (approximately 1,000 people nationally) (see also Figure 4-3). No PWSs reported detections at levels > ½ HRL or > HRL. Detection frequencies are higher for ground water systems when compared to surface water systems, as surface water systems reported zero detections. For samples with detections, the median and 99th percentile concentrations are 0.10 µg/L. These figures are identical because for metribuzin, Washington was the only state that reported a detection (0.10 µg/L) and thus this statistic is both the median and 99th percentile concentration.

Because metribuzin's low occurrence yields an underestimate from cross-section states, all data are used, even the biased data, to present a conservative upper bound estimate. Conservative estimates of metribuzin occurrence using all of the Round 2 reporting states still show relatively low detection frequencies (Table 4-4). Approximately 0.28% of PWSs (estimated at 182 PWSs nationally) experienced detections > MRL, while no PWSs experienced detections > ½ HRL, and > HRL. These figures indicate that about 1.61% of the population is affected by concentrations > MRL (approximately 3.4 million people nationally), and 0% of the population is affected by concentrations > ½ HRL or > HRL. The proportion of surface water PWSs with detections is greater than ground water systems. The median and 99th percentile concentrations of detections are 1 µg/L and 3 µg/L, respectively.

The Round 2 reporting states and the Round 2 national cross-section show a proportionate balance in PWS source waters compared to the national inventory. Nationally, 91% of PWSs use ground water (and 9% surface waters); Round 2 national cross-section states show 88% use ground water (and 12% surface waters); Round 2 reporting states show 87% use ground water (and 13% surface waters). The relative populations served are not as comparable. Nationally, about 40% of the population is served by PWSs using ground water (and 60% by surface water). For the Round 2 cross-section, 29% of the cross-section population is served by ground water PWSs (and 71% by surface water). For all Round 2 reporting states, 26% of the population is served by ground water PWSs (and 74% by surface water). The resultant national extrapolations are not additive as a consequence of these disproportions (Table 4-4).

Occurrence in the Corn Belt

SDWA compliance monitoring data from the corn belt states of Illinois, Indiana, and Ohio also show very low occurrence of metribuzin. The pesticide was not detected above the Health Reference Level in any case, and the highest 99th percentile concentration of detections among the three states was for Illinois at 0.7 µg/L (Table 4-5). Illinois also had the highest

Table 4-5. SDWA Compliance Monitoring Data from the States of Illinois, Indiana, and Ohio.

Frequency Factors	Illinois[1]	Indiana[2]	Ohio[3]
Total Number of Samples	14,818	1,033	4,039
Percent of Samples with Detections	0.2%	0.1%	0.0%
99th Percentile Concentration (all samples)	< (ND)	< (ND)	< (ND)
Health Reference Level	91 µg/L	91 µg/L	91 µg/L
Minimum Reporting Level (MRL)	Variable[4]	Variable[4]	Variable[4]
99th Percentile Concentration of Detections	0.7 µg/L	0.2 µg/L	0 µg/L
Median Concentration of Detections	0.2 µg/L	0.2 µg/L	0 µg/L
Minimum Concentration of Detections	0.1 µg/L	0.2 µg/L	0 µg/L
Total Number of PWSs	1,139	392	2,178
Number of GW PWSs	1,030	345	2,017
Number of SW PWSs	109	47	161
Occurrence by System			
% PWSs with detections (>MRL)	0.97%	0.26%	0.00%
GW PWSs with detections	0.10%	0.29%	0.00%
SW PWSs with detections	9.17%	0.00%	0.00%
% PWSs > ½ Health Reference Level	0.00%	0.00%	0.00%
GW PWSs > ½ Health Reference Level	0.00%	0.00%	0.00%
SW PWSs > ½ Health Reference Level	0.00%	0.00%	0.00%
% PWSs > Health Reference Level	0.00%	0.00%	0.00%
GW PWSs > Health Reference Level	0.00%	0.00%	0.00%
SW PWSs > Health Reference Level	0.00%	0.00%	0.00%

1 After an independent analysis of Illinois SDWA compliance monitoring data from 1993-1997 (U.S. EPA, 1999).
2 After an independent analysis of Indiana SDWA compliance monitoring data from 1993-1997 (U.S. EPA, 1999).
3 Summary results based on analysis of Ohio data from the SDWIS/FED UCM (1993), Round 2.
4 See text for discussion.
- PWS = Public Water Systems; GW = Ground Water; SW = Surface Water; MRL = Minimum Reporting Level (for laboratory analyses);
- HRL = Health Reference Level, an estimated health effect level used for preliminary assessment for this review
- The Health Reference Level (HRL) used for metribuzin is 91 µg/L. This is a draft value for working review only.
- Total Number of Samples = the total number of analytical records for metribuzin
- 99th Percentile Concentration = the concentration value of the 99th percentile of either all analytical results or just the detections (in µg/L)
- Median Concentration of Detections = the median analytical value of all the detections (analytical results greater than the MRL) (in µg/L)
- Total Number of PWSs = the total number of public water systems with records for metribuzin
- % PWS with detections, % PWS > ½ Health Reference Level, % PWS > Health Reference Level = percent of the total number of public water systems with at least one analytical result that exceeded the MRL, ½ Health Reference Level, or Health Reference Level, respectively

maximum concentration at 20 µg/L, still well below the HRL (after U.S. EPA, 1999). SDWA compliance monitoring from Iowa for the years 1988-1995 show similar results, although the data are not presented in Table 4-5 because they were not compiled at the system level in the same manner. Approximately 0.8% of samples analyzed for metribuzin in Iowa drinking water had detections of the compound with a maximum concentration of 1.6 µg/L. The 99th percentile concentration of all samples was a non-detect (Hallberg et al., 1996).

Metribuzin detection frequencies are generally much greater in surface water when compared to ground water (Tables 4-5 and 4-6). Two exceptions are the Iowa SDWA compliance data, in which surface and ground water detection frequencies are essentially the same (0.77% and 0.76%, respectively), and the Indiana SDWA compliance data which had no metribuzin detections in surface water (Table 4-5).

Table 4-6 presents data from a number of national and state drinking water monitoring studies with results in corn belt states. The National Pesticide Survey reports no detections for metribuzin. Compliance monitoring from Ohio surface water PWSs show the highest detection frequency of metribuzin by system (79.9%), but the data are from a targeted study of sensitive surface waters so results may not be representative. The highest reported concentration of the studies summarized in Table 4-6, 3.7 µg/L, is well below the HRL. Environmental Working Group reports were reviewed; however only, preliminary results were available from a special study of finished tap water in 29 cities. Metribuzin was found in unspecified concentrations in 7% (2) of the 29 cities (Cohen et al., 1995).

The Iowa State-Wide Rural Well-Water Survey established a statistically significant correlation between increasing well depth and decreasing pesticide contamination, as evidenced by the lower detection frequency of metribuzin in drinking water wells ≥50 ft deep (Table 4-6). Comparisons between raw and finished water in Iowa show detection frequencies of metribuzin in surface water increased from the raw to finished state (Table 4-6; Hallberg, 1989). This is probably a result of either analytical variance, imprecise matching between raw and finished water samples, or pesticide adsorption to and subsequent release from, filtration/treatment materials (Hallberg, 1989).

Regional Patterns

Occurrence results are displayed graphically by state in Figures 4-2 and 4-3 to assess whether any distinct regional patterns of occurrence are present. Thirty-four states reported Round 2 data but 10 of those states have no data for metribuzin (Figure 4-2). Another 21 states did not detect metribuzin. The remaining 3 states detected metribuzin in drinking water and are located on the east and west coasts of the United States (Figure 4-2). In contrast to the summary statistical data presented in the previous section, this simple spatial analysis includes the biased Massachusetts data.

Table 4-6. Metribuzin Occurrence in Midwest Drinking Water.

	% sites ≥MRL	% samples ≥MRL	maximum concentration (µg/L)
Ground Water Surveys			
National Pesticide Survey (1988-90)[1]	nd	nd	nd
Iowa State-Wide Rural Well-Water Survey [2]			
Wells < 50 ft deep	3.0%	nr	0.43
Wells ≥ 50 ft deep	1.4%	nr	0.72
Special Surface Water Studies			
Raw water			
Iowa (1986)[3]	nr	7.0%	0.89
Illinois (1985-87)[3]	nr	15.0%	3.70
Finished water			
Ohio (1993-)[4]	79.9%	22.3%	1.8
Iowa (1986)[3]	nr	12.0%	0.45

[1] U.S. EPA, 1990 ; data are national results including some Midwestern states
[2] Kross et al., 1990
[3] cited in Hallberg, 1989
[4] U.S. EPA, 1999
- HRL = 91 µg/L
- MRLs vary by study.
- nd = results below the respective reporting level
- nr = "not reported"

The simple spatial analysis presented in Figures 4-2 and 4-3 does not suggest any special regional patterns. Further, use and environmental release information (Chapter 3) and ambient water quality data (Section 4.1) indicate that metribuzin has low detection even in non-drinking water sources. According to TRI data, industrial releases have occurred since 1995 in only three states and one U.S. territory (IA, MO, NB, Puerto Rico; U.S. EPA, 2000b). However, the use patterns for metribuzin (Figure 3-1) do show that use is concentrated in soybean producing regions (similar to the corn belt) in the Midwest states and along the Mississippi River Valley production region. These states are missing from the Round 2 data, hence, a special review was conducted to evaluate data from Iowa, Illinois, Indiana, and Ohio. Occurrence rates in these states are much greater than other areas, but even in these states no PWSs had results > HRL.

Figure 4-2. States with PWSs with Detections of Metribuzin for All States with Data in SDWIS/FED (Round 2).

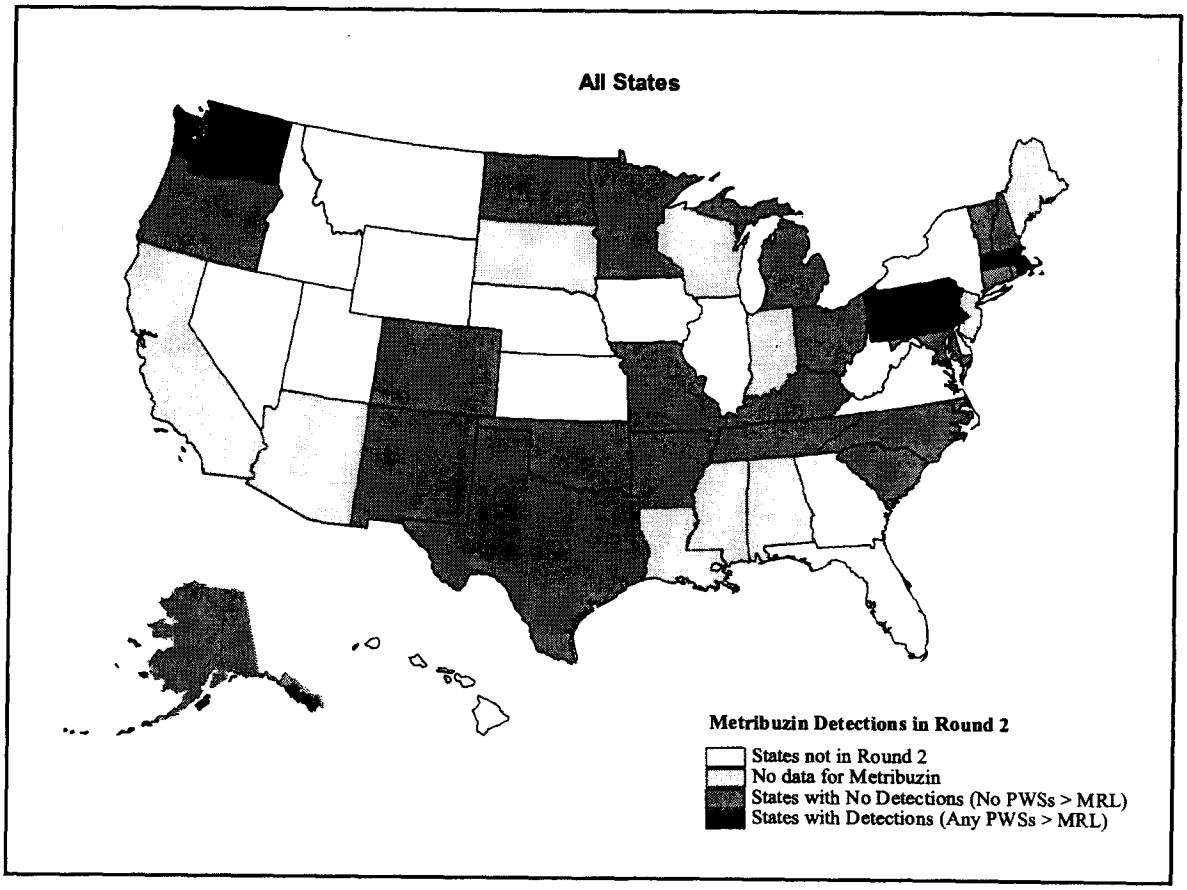
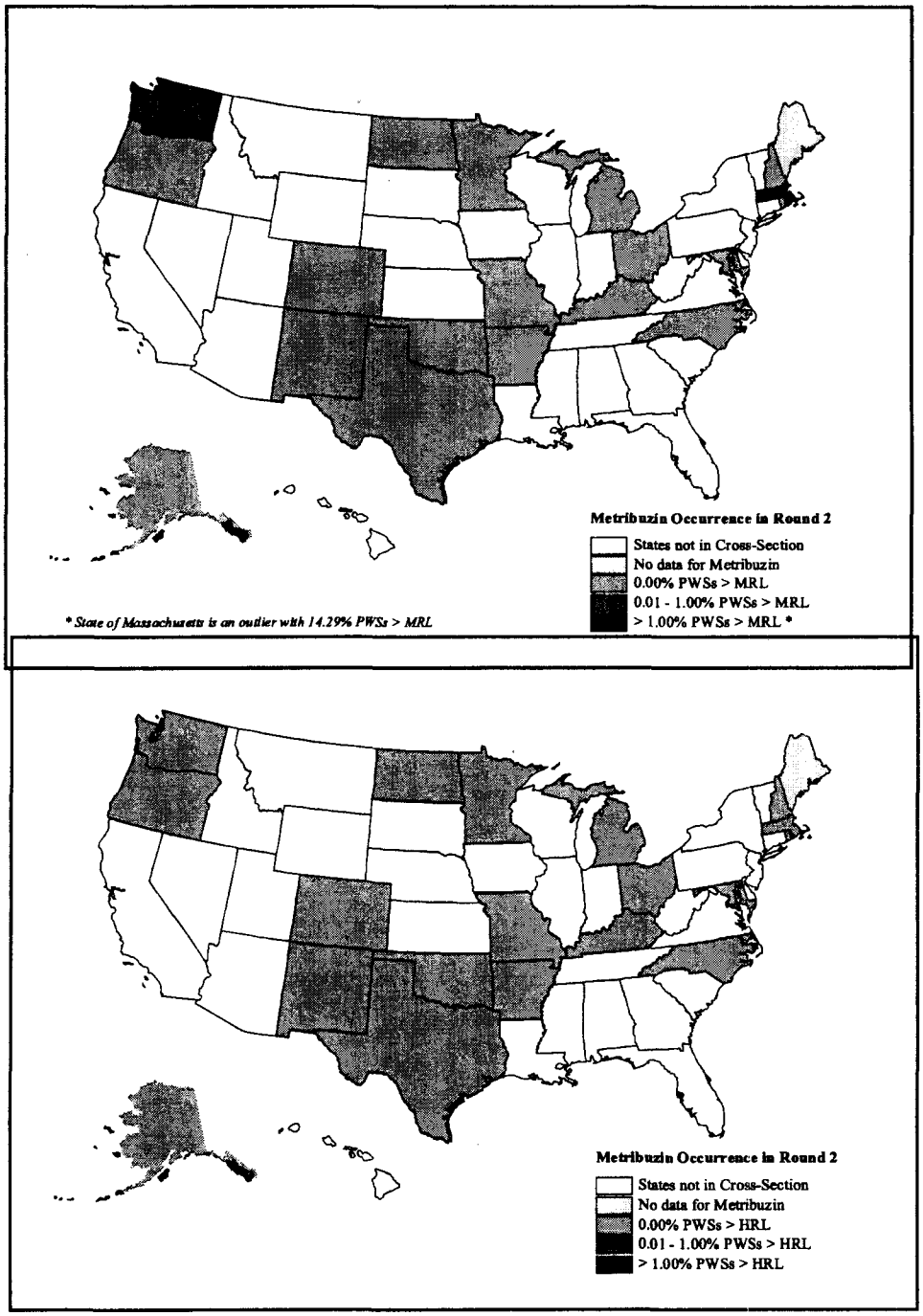


Figure 4-3. Round 2 cross-section states with PWSs with detections of metribuzin (any PWSs with results greater than the Minimum Reporting Level [MRL]; above) and concentrations greater than the Health Reference Level (HRL; below).



4.3 Conclusions

Detection frequencies and concentrations of metribuzin in ambient surface and ground water are low, especially in ground water. Even so, it is one of the 21 most commonly detected pesticides in ground water from the first round of NAWQA intensive data collection. The annual mean frequency of metribuzin detection in surface water was less than 15% for all land-use settings and concentrations. Midwestern ambient surface and ground water concentrations and detection frequencies are also low. Releases of metribuzin to the environment were reported in the TRI from only three states and one territory.

Metribuzin has been detected in PWS samples collected under the Safe Drinking Water Act (SDWA). Cross-section occurrence estimates are very low with only 0.003% of all samples showing detections. Significantly, the values for the 99th percentile and median concentrations of all samples are less than the Minimum Reporting Level (MRL). For the Round 2 cross-section samples with detections, both the median and the 99th percentile concentrations are 0.10 µg/L. Systems with detections constitute approximately 0.007% of Round 2 cross-section systems. National estimates for the population served by PWSs with detections using the cross-section data are also low: approximately 1,000 people (about 0.0003% of the national PWS population) are served by PWSs with metribuzin detections > MRL, and no PWSs reported detections > ½ HRL or > HRL. Using more conservative estimates of occurrence from all states reporting SDWA Round 2 monitoring data, including states with biased data, 0.28% of the nation's PWSs (approximately 182 systems and 3.4 million people served) are affected by metribuzin concentrations > MRL, while no PWSs are affected by concentrations > ½ HRL or > HRL.

The heaviest use of metribuzin is across the nation's corn-soybean production area. These states are not well represented in the Round 2 database. Therefore, additional data from the Midwest corn belt were also evaluated. Drinking water data from the corn belt states of Iowa, Indiana, Illinois, and Ohio also show very low occurrence of metribuzin. Special targeted surface water studies from Ohio have the highest detection frequency of metribuzin (79.9% of systems). The pesticide was not detected above the Health Reference Level in any sample, with the highest concentration at 20 µg/L.

5.0 EXPOSURE FROM MEDIA OTHER THAN WATER

This section summarizes human population exposures to metribuzin from food, air, and soil. The primary purpose is to estimate average daily intakes of metribuzin by members of the general public. When exposure data on subpopulations were located, such as occupationally exposed persons, these data were also summarized and included in this section.

5.1 Exposure from Food

5.1.1 Exposures of the General Population

Concentrations of Metribuzin in Food Items

Metribuzin is a triazine herbicide used to control small seeded grasses and broadleaf weeds in crops such as soybeans, potatoes and sugarcane (Bouchard, 1982). Several studies have evaluated its residues in food (as mentioned below). However, not all studies may be representative of concentrations that the general population would typically be exposed to from food items. In the animal studies summarized below, metribuzin concentrations administered in feed were greater than those that would occur under typical feeding conditions. In the plant studies summarized below, metribuzin residues in plant tissues and food products were measured at the point of application. During the time lapse between food production and consumption by the general public, metribuzin may further be metabolized and dissipated in the food product, and also be removed through washing and food preparation. Thus, the metribuzin concentrations reported in some studies are most likely higher than those that the general population would encounter in their diets.

In 1999, approximately 9,438 domestically produced and imported food samples were analyzed for 366 different pesticides as part of the Food and Drug Administration's (FDA) Regulatory Monitoring Program. Metribuzin was not detected (detection limit not reported) in any samples of grains, milk products, fruits or vegetables. Metribuzin was also not detected (detection limit not reported) in any of the 218 domestic or 298 imported fish and shellfish samples analyzed (US FDA, 1999).

One study examined the uptake and metabolism of metribuzin in soybeans. After a pre-emergence soil application of ^{14}C-metribuzin at 0.3 lb ai/A (active ingredient/acre), soybean plants and mature soybean seeds contained total radioactive residues (expressed as metribuzin equivalents) of 12.1 ppm (mg/kg) and 0.48 ppm (mg/kg), respectively. The major metribuzin metabolite in both soybean plants and mature seeds was the 6-(1,1-dimethylethyl)-3,5-(diketo)-1,2,4-triazin-5-(2 H,4H)-dione (DADK) (U.S. EPA, 1998a).

Growth chamber experiments measured metribuzin absorption and distribution in soybean plants during a 6-day period after emergence. Soybean plants grown in soils treated with 0.28 kg/ha (kg/hectare) ^{14}C-metribuzin contained metribuzin concentrations ranging from 8.86 to 9.99

µg/g (mg/kg) metribuzin. Shoot concentrations were not as high as those in roots, and little radioactivity was found in leaves of plants (Hardgroder and Rogers, 1974).

Post-emergence treatment of wheat with 5-^{14}C-metribuzin at 0.15 lb ai/acre resulted in 0.2 ppm (ppm, expressed as metribuzin equivalents) total radioactive residues in wheat grains after 33 days. About 9.3% of these residues consisted of metribuzin and its metabolites (U.S. EPA, 1998a).

Field studies conducted in California, Delaware, Illinois, Michigan, New Jersey, Texas and Washington evaluated metribuzin residues in carrots after post-emergence herbicide treatment. Metribuzin and metribuzin metabolite residues in carrots were below the EPA tolerance level of 0.3 ppm after multiple applications of up to four times the maximum allowable rate (U.S. EPA, 1998a).

Cessna (1998) measured metribuzin residues in lentil crops in Canada. After post-emergence application of 0.28 kg/ha, lentils contained residues of 1 mg/kg metribuzin. Residues in lentils decreased five- and ten-fold after one and two weeks, respectively, and were not detected after six weeks. At lentil maturity, metribuzin was below the detection limit of 0.02 mg/kg.

A ruminant (goat) metabolism study evaluated the distribution of metribuzin and its metabolites in various tissues (U.S. EPA, 1998a). Goats were administered 410 ppm 5-^{14}C-metribuzin by diet for three consecutive days. This corresponds to approximately 59 times the calculated dietary burden of metribuzin for ruminants. Total radioactive residues reported in various tissues were 2.66 mg/kg in liver, 4.27 mg/kg in kidney, 0.97 mg/kg in fat, 0.44 mg/kg in muscle, and 0.25-2.09 mg/kg in milk (U.S. EPA, 1998a). Because animals were administered metribuzin in their diets at concentrations of up to 59 times their dietary burden, the resulting tissue residues may tend to be up to 59 times higher than those that would occur under typical feeding conditions.

In a poultry metabolism study, hens were given feed at a concentration of 400 ppm 5-^{14}C-metribuzin for three days. This corresponds to approximately 500 times the calculated dietary burden of metribuzin for poultry. Radioactive residues of 33.6 mg/kg in liver, 36.3 mg/kg in kidney, 1.6 mg/kg in muscle, and 0.2-1.0 mg/kg in eggs were reported (U.S. EPA, 1998a). Because animals in this study were administered metribuzin in their diets at concentrations of up to 500 times their dietary burden, the resulting tissue residues may tend to be up to 500 times higher than those that would occur under typical feeding conditions.

Intake of Metribuzin from Food Items

From the studies mentioned above, the analysis of metribuzin in food items conducted by the FDA Regulatory Monitoring Program appears to be most representative of general population exposures to metribuzin in food items. Although additional studies reporting metribuzin residue levels in food items were identified, these studies were conducted at dietary concentrations that

are higher than anticipated to occur under typical herbicide use conditions. Metribuzin was not detected in 9,438 domestic and imported food items analyzed during FDA pesticide regulatory monitoring (US FDA, 1999). Based on this, the typical average daily intake of metribuzin from food for the general population is anticipated to be close to zero.

Both imported and domestic fish and shellfish samples analyzed for pesticides during FDA regulatory monitoring did not contain metribuzin at detectable levels (US FDA, 1999). Based on this, the typical average daily intake of metribuzin from fish and shellfish for the general population is anticipated to be close to zero.

5.1.2 Exposures of Subpopulations

No evidence was located in the available literature indicating the existence of subpopulations with dietary intakes of metribuzin different from those of the general population.

5.2 Exposure from Air

5.2.1 Exposures of the General Population

Concentrations of Metribuzin in Air

Information on ambient levels of metribuzin measured in air were not located in the available literature.

Intake of Metribuzin from Air

Concentration data on ambient levels of metribuzin were unavailable to estimate average intakes by the general population from air. However, based upon its physical properties, metribuzin is not expected to be present in ambient air. Metribuzin is a solid at ambient temperatures, and has a low vapor pressure (4.4×10^{-7} mm Hg at 20°C). Therefore, it is not likely to readily partition into ambient air. Additionally, any partitioning of metribuzin into air would most likely occur in areas where it is used. These areas are typically agricultural regions, remote from the general population. Based upon this, ambient air concentrations of metribuzin are most likely close to zero. Thus, the typical average daily intake for the general population is anticipated to be close to zero.

5.2.2 Exposures of Subpopulations

Concentrations of Metribuzin in Air

Occupational exposures to metribuzin may occur as part of its regular use. Persons involved in mixing, loading, applying or handling the various dry and liquid formulations of metribuzin during its ground and aerial applications have the potential to be exposed. Concentration data for metribuzin in air were not obtained from the available literature.

However, the EPA has estimated baseline inhalation exposures for workers involved in the regular use of metribuzin as a herbicide ranging from 0.006 to 91.14 mg/day (U.S. EPA, 1998a). The greatest inhalation exposure estimates are for persons involved in the handling of powdered and dry bulk forms of metribuzin. The estimated daily inhalation exposure for a person mixing wettable powder for application to sugarcane crops is 91.14 mg/day, and 31.3 mg/day for a worker loading or mixing dry bulk fertilizer. The lowest daily inhalation exposures (0.006 mg/day) were seen in workers involved in the liquid applications of metribuzin to turf grass by plane (U.S. EPA, 1998a).

Intake of Metribuzin from Air

The EPA estimated inhalation exposures for workers involved in the regular use of metribuzin to range from 0.006 to 91.14 mg/day (U.S. EPA, 1998a). Dividing these estimates by a body weight of 70 kg results in daily metribuzin intakes for adult workers ranging from 8.6×10^{-5} to 1.3 mg/kg-day.

5.3 Exposure from Soil

5.3.1 Exposures of the General Population

Concentrations of Metribuzin in Soil

Information was not located regarding metribuzin levels in residential soils. Metribuzin is not labeled for residential use by homeowners or certified applicators. Thus, it is not anticipated to be found in residential soils.

Intake of Metribuzin from Soil

Based on its approved uses, exposure to metribuzin in soil is not anticipated to be a typical route of exposure for the general population. Because metribuzin is not labeled for residential use by homeowners or certified applicators, the intake of metribuzin through soil by most of the general population is probably close to zero.

5.3.2 Exposures of Subpopulations

Concentrations of Metribuzin in Soil

Several studies (Burgard et al., 1994; Brown et al., 1985; Dao, 1995; Gallaher and Meuller, 1996) have reported metribuzin levels in agricultural soils, which may be a source of occupational exposure for those involved in the handling or application of this chemical. Soil concentrations were dependant upon application rate, and decreased over time following application. At application rates ranging from 0.56 to 1.1 kg/ha, initial metribuzin concentrations in soil ranged from 0.09 to 0.78 mg/kg. After 86-195 days, concentrations ranged from 0.007 to 0.11 mg/kg.

Post-application exposures to metribuzin in soil may occur for persons entering areas that have been treated with metribuzin. The general public may be exposed after the application of metribuzin to turfgrass in public areas (e.g. parks, athletic fields, or golf courses) that have been treated with metribuzin (U.S. EPA, 1998a). Specific information on post-application concentrations in recreational areas or exposure estimates were not available in the obtained literature.

Intakes of Metribuzin from Soil

At an application rate of 0.56 kg/ha, metribuzin concentrations in soil may be as high as 0.78 mg/kg upon first application, with levels decreasing over time (Gallaher and Mueller, 1996). At this concentration, and a daily soil intake of 480 mg/day for a contact intensive worker (U.S. EPA, 1997), the maximum total daily intake of metribuzin for a 70 kg adult worker would be 5.3×10^{-3} mg/kg-day.

5.4 Other Residential Exposures

Metribuzin may be transported from agricultural fields during runoff events. Sediment in run-off water from winter wheat fields in eastern Washington contained metribuzin concentrations ranging from below detection limits (200 µg/kg sediment) to 3440 µg/kg wet weight (Brown et al., 1985). These samples were collected from three major runoff events during 1979-1980 that produced more than 7.5 grams of sediment. Run-off samples generating less than 7.5 grams of sediment were not analyzed for metribuzin in this study. Metribuzin concentrations in 18 run-off water samples ranged from below detection limits (5 µg/L) to 44 µg/L.

An additional study evaluated metribuzin concentrations in surface runoff samples collected from midwestern streams during the first major runoff event after its application. The 90th percentile concentrations of metribuzin collected in 1989, 1994, and 1995 were 1.4, 1.2, and 0.5 ppb, respectively (U.S. EPA, 1998a).

5.5 Summary

Concentration and intake values for metribuzin in media other than water to the general population and an occupationally exposed adult subpopulation are summarized in Tables 5-1 and 5-2. Based on the available information, the general population, on average, is not typically expected to be exposed to metribuzin from food, air or soil. However, for persons who are occupationally exposed to metribuzin, inhalation appears to be the main route of exposure to this chemical.

Table 5-1. Exposures of the General Population to Metribuzin in Media Other Than Water.

Parameter	Medium					
	Food		Air		Soil	
	Adult	Child	Adult	Child	Adult	Child
Concentration in medium	not detected	not detected	NA		NA	
Estimated daily intake (mg/kg-day)	0.0*	0.0*	0.0*	0.0*	0.0*	0.0*

NA= Not Available in literature

* expected to be close to zero based upon physical properties and/or use of chemical (see Sections 5.1.1, 5.2.1 and 5.3.1)

Table 5-2. Exposures of Subpopulations to Metribuzin in Media Other Than Water.

Parameter	Medium		
	Food	Air	Soil
	Adult Worker	Adult Worker	Adult Worker*
Concentration in medium	NA	0.006 to 91.14 mg/day	0.78 mg/kg
Estimated daily intake (mg/kg-day)	--	8.6×10^{-5} to 1.3 ** mg/kg-day	5.3×10^{-3}*** mg/kg-day

NA= Not Available in literature.

-- = Unable to estimate based on available information

* Estimates are for a contact intensive worker, with direct soil contact.

** Based on U.S. EPA (1998a) estimates for inhalation exposures of workers handling or applying metribuzin (see Section 5.2.2).

***High-end estimate based upon maximum soil concentration after application.

6.0 TOXICOKINETICS

6.1 Absorption

Based on urinary excretion data, 36-52% of orally administered metribuzin was absorbed in Sprague-Dawley rats (U.S. EPA, 1993). In dogs, 52-60% of the administered oral dose was absorbed (U.S. EPA, 1993). However, in a recent study, Mathew et al. (1998) reported poor absorption (< 15%) of metribuzin in Sprague-Dawley rats fed extracts of soybean plants containing ^{14}C-metribuzin for 2 days (6,392-156,000 disintegrations per minute/g body weight).

6.2 Distribution

Mathew et al. (1998) reported on the distribution of ^{14}C-metribuzin in Sprague-Dawley male rats (n=4) after a 2-day feeding with a normal rat chow containing a methanol extract of beans and shoots of soybean plants radiolabeled with metribuzin (6,392-156,000 dpm/g body weight). There was no radioactivity detected in tissues such as heart, kidney, and liver, suggesting that the metabolites of metribuzin, or the parent compound, are not accumulated.

6.3 Metabolism

Animal studies suggest that metribuzin undergoes deamination and deketonization during its metabolism. The presence of metribuzin metabolites, diketo metribuzin and deaminated-diketo metribuzin in urine was also reported (U.S. EPA, 1993). In a study conducted by Cain et al. (1987), the authors reported the metabolism of metribuzin in rats to involve deamination, dethioalkylation, hydroxylation of the t-butyl side chain and conjugation with glutathione.

6.4 Excretion

Studies in Wistar rats performed by Cain et al. (1987) used either a single low dose (5 mg/kg) of ^{14}C-metribuzin (98.4-99.4% active ingredient; Specific Activity 20.8 mCi/nmol), or a single high dose (500 mg/kg). No significant changes were observed in the rates or the routes of ^{14}C-elimination between male and female rats in either the low-dose or high-dose administration groups. In general, 27.3-43.4% of the radiolabel was excreted in the urine and from 55.8 to 71.5% of the radiolabel was excreted in feces after 96 hours.

About 90% of administered metribuzin in rats was excreted within 16 days in one study or within 5 days by another. The half-life for elimination of radiolabeled metribuzin was reported as 19.1-30.4 hours for male rats and 22.4-33.6 hours for female rats (U.S. EPA, 1993). Moreover, in dogs, over 90% of the oral dose was excreted between 72 and 120 hours, with about 52-60% excreted in the urine as metabolites or conjugates and about 30% excreted in the feces predominantly as unchanged metribuzin (U.S. EPA, 1993).

Mathew et al. (1998) reported that approximately 85% of the radioactivity was eliminated in the feces of rats 4 days after a 2-day feeding with extracts of soybean plants containing radiolabeled metribuzin. About 1-8% of the radioactivity was eliminated in the urine.

7.0 HAZARD IDENTIFICATION

7.1 Human Effects

7.1.1 Short-Term Studies

There are no short-term studies available which report the effect of metribuzin on human health.

7.1.2 Long-Term and Epidemiological Studies

There are no long-term epidemiological studies available which have examined the relationship between exposure to metribuzin and human health effects.

7.2 Animal Studies

7.2.1 Acute Toxicity

Animal studies have demonstrated that metribuzin exposure induces low acute toxicity. The doses of metribuzin that cause acute toxic effects are summarized in Table 7-1 (U.S. EPA, 1998a). Kimmerle et al. (1969) found that metribuzin was not an eye irritant in a primary eye irritation test in rabbits. In a primary dermal irritation study also conducted by Kimmerle et al. (1969), metribuzin exposure produced very slight irritation of rabbit skin. However, metribuzin exposure has not been shown to produce sensitization effects in guinea pigs (ACGIH, 1986).

7.2.2 Short-Term Studies

There are no short-term animal studies available which have examined the relationship between metribuzin exposure and adverse health effects.

7.2.3 Subchronic Studies

Flucke and Hartmann (1989) evaluated systemic and dermal toxicity in New Zealand rabbits (HC:NZW strain) that were dermally exposed to metribuzin (DIC 1468, technical 94%) at 0, 40, 200, or 1,000 mg/kg-day (6 hours/day; 5 days/week) for 3 weeks. Neither dermal irritation nor mortality were observed in the study. However, high-dose males and females did demonstrate a dose-related increase in cholesterol. Triiodothyronine (T3) was decreased in all males, but this decrease was statistically significant only at the high dose. The authors reported statistically significant increases in liver enzymes such as N-demethylase and cytochrome P450 activities in high-dose males.

Chaisson and Cueto (1970) studied toxic effects in Beagle dogs (4 animals/sex/group) orally fed metribuzin in the diet at 0, 50, 150 or 500 ppm for 90 days. No differences in body

Table 7-1. Acute Toxic Effects of Metribuzin

Species	Active Ingredient	Route of Exposure	Results	Reference
Rats	Not Specified	Oral	LD_{50}: 1,100 mg/kg	Morgan, 1982
Rats	Technical (% not specified)	Oral	LD_{50}: Males 1,090 mg/kg Females 1,206 mg/kg	Crawford and Anderson, 1974
Rat	Not Specified	Oral	LD_{50}: Males 2,379 mg/kg Females 2,794 mg/kg	Mobay Chemical, 1978a
Rat	Not Specified	Oral	LD_{50}: Males 2,300 mg/kg Females 2,200 mg/kg	Kimmerle et al.,1969
Mouse	Not Specified	Oral	LD_{50}: 698-711 mg/kg	Hartley and Kidd, 1987
Cat	Not Specified	Oral	LD_{50}: > 500 mg/kg	Hartley and Kidd, 1987
Guinea Pig	Not Specified	Oral	LD_{50}: Males 245 mg/kg Females 274 mg/kg	Crawford and Anderson, 1974
Guinea Pig	Not Specified	Oral	LD_{50}: 250 mg/kg	Hartley and Kidd, 1987
Rat and Rabbit	Not Specified	Dermal	LD_{50}: > 2,000 mg/kg	ACGIH, 1986
Rabbit	Technical (% not specified)	Dermal	LD_{50}: > 20,000 mg/kg	Crawford and Anderson, 1972
Rat	Not Specified	Percutaneous	LD_{50}: > 20,000 mg/kg	Hartley and Kidd, 1987
Rat	Not Specified	Dermal	LD_{50}: > 5,000 mg/kg	Mobay Chemical, 1978a
Mouse	Not Specified	Inhalation	LC_{50}: > 860 mg/m^3	ACGIH, 1986
Rat	Not Specified	Inhalation	LC_{50}: > 20,000 mg/m^3	Mobay Chemical, 1978a
Rat	92.6%	Inhalation	LC_{50}: > 648 mg/m^3	Shiotsuka, 1986
Mouse	Not Specified	Intraperitoneal	LD_{50}: 210 mg/kg	PCBPBS, 1984

weight gain or food consumption were observed at any of the doses tested. However, in both male and female animals, dose-related increases in liver weight, and liver:body weight and liver:brain weight ratios, were reported. Blood chemistry analysis did not reveal any differences between the control and treated groups, except a small decrease in SGOT (serum glutamate-oxaloacetate transaminase) and SGPT (serum glutamate-pyruvate transaminase) activities in the high-dose male group at the end of the study. These findings implicate the liver as a possible target organ. However the dose levels were not verifiable.

Loser et al. (1969) reported toxic effects in Wistar rats (5 animals/sex/group) fed metribuzin at 0, 50, 150, 500 or 1,500 ppm for three months. The authors observed no statistically significant changes in food consumption; however, there was a significant reduction in body weight gain and an increase in liver and thyroid weights observed in the high-dose (1,500 ppm) group. Pathology in the lung and liver was unremarkable in either the control or treatment groups.

In studies conducted by Lindberg and Richter (1970), Beagle dogs (four/sex/dose) which were administered oral doses of 50, 150 or 500 ppm (about 1.25, 3.75 or 12.5 mg/kg-day, based on dietary assumptions of Lehman, 1959) of technical metribuzin for 90 days showed no significant differences in body weights, food consumption, behavior, mortality, hematological findings, urinalysis, gross pathology or histopathology.

In a study reported by ACGIH (1986), no effects were observed during a 3-week period of daily dermal application of 1,000 mg metribuzin/kg. A 3-week inhalation study conducted in rats (ACGIH, 1986) (aerosol exposure six hours daily, 5x/week) at an air concentration of 31 mg/m^3 was without observable effects.

In a 21-day inhalation toxicity study, Thyssen (1981) administered metribuzin (DIC 1468, 93.1-98.2% active ingredient) at doses ranging from 0-720 mg/m^3 daily for 6 hours. Increased N-demethylase, O-demethylase and cytochrome P450 activities along with increased liver and thyroid weights were noted in the high dose (720 mg/m^3) group.

7.2.4 Neurotoxicity

There are no studies available which correlate exposure to metribuzin with neurotoxic effects.

7.2.5 Developmental/Reproductive Toxicity

In a developmental toxicity (teratology) study, metribuzin (92.6% active ingredient) was administered to pregnant Charles River rats (Crl:CD BR) in doses of 0, 25, 70 or 200 mg/kg-day by gavage on gestation days 6-18. Maternal toxic effects such as a reduction in body weight gain during the entire gestation period, and a decrease in food consumption, were observed at all doses. The high-dose (200 mg/kg-day) group showed a statistically significant increase in thyroid weight. A decrease in thyroxine (T4) levels was reported in both the 70 and 200 mg/kg-day dose

groups (Kowaski et al., 1986). In another developmental toxicity study, Machemer (1972) reported a reduction in maternal weight gain only in the high-dose rat group (FB 30 Strain) fed metribuzin at 0, 5, 15, 50 and 100 mg/kg-day during gestation period days 6-15. No evidence of fetal toxicity was reported in the rats administered metribuzin at doses of 100 mg/kg-day or below.

In a 3-generation reproduction study, Loser and Siegmund (1974) administered technical metribuzin in the feed at dose levels of 0, 35, 100 or 300 ppm (about 0, 1.75, 5 or 15 mg/kg-day, based on dietary assumptions of Lehman, 1959) to FB30 (Elberfeld breed) rats during mating, gestation and lactation. Following treatment, fertility, lactation performance, and pup development were evaluated. No treatment-related effects were reported at any dose tested.

In a developmental toxicity (teratology) study conducted by Clemens and Hartnagel (1989), American Dutch rabbits (17 females/dose group) were dosed with 0,10, 30 or 85 mg/kg-day of metribuzin (92.7% active ingredient) by gavage on gestation days 6-18. Maternal toxicity was noted at doses of 30 mg/kg-day and above, based on a reduction in maternal body weight gain on gestation days 18-28, and a decrease in food consumption on gestation days 7-19 at the high-dose level. A no-observable-adverse-effects-level (NOAEL) for maternal toxicity was determined to be 10 mg/kg-day and a maternal lowest-observable-adverse-effects-limit (LOAEL) of 30 mg/kg-day.

In another developmental toxicity (teratology) study, New Zealand white rabbits were administered 0, 15, 45, or 135 mg/kg-day of metribuzin by gavage on gestation days 6-18. Maternal systemic toxicity was noted at 45 mg/kg-day as reduced body weight gain, and reduced food and water intake. Additionally, at 135 mg/kg-day there was an increased incidence of abortions and decreased body weights. There were no significant differences between control and treatment groups reported for the mean number of corpus lutea, implantation sites, early or late resorptions, and live or dead fetuses (Unger and Shellenberger, 1981).

In a two-generation reproduction study conducted by Porter et al. (1988), Cr:CD BR rats were exposed orally via diet, with 0, 30, 150 or 750 ppm of metribuzin (Sencor® technical 92.6% active ingredient). Compared to the control animals, the high-dose adult males and females of both the F_0 and F_1 generations consumed less food and gained less body weight. Necropsy findings on both the F_0 and F_1 generations were not affected by the metribuzin treatment. There were no treatment related effects observed in the pathology of the reproductive organs or the pituitary tissues. However, a dose-related increase in the hypertrophy of the hepatocytes of the centrilobular and mid zonal regions was noted in the high-dose (750 ppm) males and mid- and high-dose (150 and 750 ppm) females. No other biologically relevant observations were noted. Therefore, for reproductive toxicity and systemic effects a NOAEL of 30 ppm and LOAEL of 150 ppm were established.

7.2.6 Chronic Toxicity

In a 2-year feeding study conducted by Loser and Mohr (1974), 40 Wistar rats/sex/group received 25, 35, 100 and 300 ppm of metribuzin (99.5% pure) in their diets; 80 rats/sex served as controls. These doses corresponded to 0, 1.3, 1.9, 5.3 and 14.4 mg metribuzin/kg/day, respectively, in the males and 0, 1.7, 2.3, 6.5 and 20.4 mg metribuzin/kg/day, respectively, in females. Metribuzin exposure resulted in no significant difference in either food consumption or mortality rate when compared to the control groups. The body weights of the rats in the 25, 35 and 100 ppm dose groups (both sexes) at the end of 2-years did not differ significantly from their respective controls. However, body weight gains in the male high-dose groups were significantly decreased during weeks 70-80 and 90-100; high-dose female body weights were significantly decreased from weeks 20-100.

Hayes (1981) investigated the systemic effects of metribuzin in a 2-year feeding study in outbred CD-1 mice. In this study, metribuzin technical (92.9% pure) dissolved in corn oil and added to a commercial diet was administered to the mice (50/sex/group) at levels of 0, 200, 800 or 3,200 ppm (about 30, 120 or 480 mg/kg-day, based on the dietary assumptions of Lehman, 1959) for 104 weeks. The body weights of the treated males (all dose groups) and females (all dose groups with the exception of 800 ppm group) did not differ significantly from those of the control group. Metribuzin treatment induced inconsistent results in the hematological parameters. Survival rates were not altered by metribuzin exposure.

In a 2-year feeding study conducted by Loser and Mirea (1974), four Beagle dogs/sex/group were administered 0, 25, 100, or 1,500 ppm (0, 0.8, 3.4 or 55.7 mg/kg-day for males; 0, 0.8, 3.6, or 55.3 mg/kg-day for females) of metribuzin (Bay 94 337 technical 99.5%) in the diet. Mortality rates were observed in the high-dose (1,500 ppm) group at 75% in both males and females. The clinical tests performed after twelve months of metribuzin exposure suggested the presence of liver dysfunction in the dogs. Elevated activities of liver enzymes such as SGOT, SGPT, OCT (ornithine-carbamyl transferase) and alkaline phosphatase along with an increase in BSP (bromsulphthalein) retention were reported in the males. Increased SGPT, OCT and serum protein levels were observed in high-dose females. There were no major changes in kidney function. An increase in thyroid weight was observed in the high-dose groups of both sexes.

Christenson and Wahle (1993) conducted a 2-year feeding study, in which Fischer 344 rats received 0, 30, 300 or 900 ppm (0, 1.3, 13.8, 42.2 mg/kg-day in males; 0, 1.6, 17.7, 53.6 mg/kg-day females) metribuzin (93.0% active ingredient) for 104 weeks. There were no major changes in the food consumption or the mortality rates observed subsequent to metribuzin exposure. A decrease in body weight gain was noticed in high-dose males (900 ppm) and mid- and high-dose females (300 and 900 ppm). Increases in brain:body weight, heart:body weight, kidney:body weight, and liver:body weight ratios were observed, in addition to increases in thyroid weights and thyroid:body weight ratios, in the high-dose groups for both sexes. In general, thyroxine (T4) levels increased in all dose levels, while triiodothyronine (T3) levels decreased at all dose levels, but no other systemic effects were observed. A significant increase in corneal neovascularization was observed in male rats receiving 300 and 900 ppm metribuzin. An incidence of macroscopic

changes in the 300 and 900 ppm metribuzin treated male rats included a discolored zone in the liver, an enlarged adrenal and thyroid gland, ocular opacity, an enlarged abdomen and epididymal mass. Ovarian cysts were detected in the 300 and 900 ppm metribuzin treated females.

7.2.7 Carcinogenicity

Hayes (1981) conducted studies in which technical metribuzin was administered in the diet to albino CD-1 mice (50/sex/dose) at 200, 800 or 3,200 ppm (approximately 30, 120 or 480 mg/kg-day) for 24 months. Although some increase in the number of tumor-bearing animals was observed in low- and mid-dose animals, significant increases in the incidence of specific tumor types were not observed at any dose level. The authors concluded that, under the conditions of the test, there was no increase in the incidence of tumors in mice.

Subsequently, statistical analysis of this data was performed by the EPA's Office of Pesticide Programs using the Chi square test (U.S. EPA, 1993). Reevaluations resulted in a statistically significant ($p=0.037$ and $p=0.045$, respectively) decrease in malignant and total tumor-bearing male mice in the high-dose group. The number of tumor-bearing female mice appeared to increase in the low-dose group (not statistically significant, $p=0.071$) and did significantly increase in the middle-dose group ($p=0.45$ for malignant tumors and $p=0.0499$ for benign tumors). The tumor incidence in high-dose females was comparable to that of the female control group. The overall conclusion drawn was that, under the test conditions in the Hayes (1981) study, metribuzin exposure did result in an increase of tumor incidence in mice.

In a 2-year feeding study by Loser and Mohr (1974), 40 Wistar rats/sex/group received 25, 35, 100 and 300 ppm metribuzin (99.5% pure) in their diets; while 80 rats/sex served as a control group. These doses corresponded to 0, 1.3, 1.9, 5.3 and 14.4 mg metribuzin/kg/day, respectively, in the males and 0, 1.7, 2.3, 6.5 and 20.4 mg metribuzin/kg/day, respectively, in females. Loser and Mohr (1974) reported through initial evaluation that there were statistically significant increases in the incidence of liver bile duct adenomas and pituitary gland adenomas in the female high-dose groups by pair-wise comparison. The incidence of bile duct adenoma in the females was 13/71, 4/10, 5/10, 1/10 and 19/35 in the control, 25, 35, 100 and 300 ppm groups, respectively, while, the incidence in males was 19/66, 10/10, 8/10, 5/10 and 9/29, respectively. The incidence of pituitary gland adenomas in the female control and high-dose groups was 27/71 and 21/35 respectively, while in males the incidences were 10/62 and 6/29, respectively. It was determined that the incidence of tumors in male rats was not significantly different in any of the tissues examined.

The EPA's Office of Pesticide Programs reevaluated the original histopathological findings reported by Loser and Mohr (1974). In this reevaluation, all of the female liver bile duct adenomas were reclassified as bile duct proliferation. The pituitary glands from all animals were also histopathologically reevaluated. It was determined that the incidences of pituitary adenoma in the female groups were 16/71 (23%), 6/34 (18%), 9/31 (29%), 11/33 (33%) and 14/35 (40%) in the control, 25-, 35-, 100- and 300-ppm groups, respectively (U.S. EPA, 1993).

In another 2-year feeding cancer study conducted by Christenson and Wahle (1993), Fischer 344 rats received 0, 30, 300 or 900 ppm (0, 1.3, 13.8, 42.2 mg/kg-day in males and 0, 1.6, 17.7, 53.6 mg/kg-day females) of metribuzin (93.0% active ingredient) for 104 weeks. The most significant change observed was thyroid follicular hyperplasia in male rats at the highest dose. There were no significant changes in the neoplastic lesions of other tissues (kidney, pituitary) observed in both the high-dose males and females. Christenson and Wahle (1993) concluded that there was no evidence of carcinogenicity in any of the tissues examined.

7.3 Other Key Data

7.3.1 Mutagenicity/Genotoxicity

Metribuzin was determined to be nonmutagenic when tested in unspecified strains of *Salmonella typhimurium* and *Escherichia coli* (Mobay Chemical Corp., 1977, 1978b). Metribuzin exposure did not induce a reverse mutation in the D7 strain of *Saccharomyces cerevisiae* either in the presence or absence of metabolic activation (Mobay Chemical Corp., 1987). Metribuzin was determined to be negative when tested for dominant lethal effects in male and female mice (unspecified strain) treated with doses of 300 mg metribuzin/kg (Mobay Chemical Corp., 1974a, 1975, 1976). It was determined that doses of 100 mg metribuzin/kg did not induce chromosomal aberrations in Chinese hamster spermatogonia (Mobay Chemical Corp., 1974b). Metribuzin exposure did not cause a significant increase in the unscheduled DNA synthesis when added to test cultures of rat primary hepatocytes (Mobay Chemical Corp., 1986a) and was determined to be negative in the CHO/HGPRT mutation assay (Mobay Chemical Corp., 1986b). However, S-9 activated (but not nonactivated) metribuzin was determined to be clastogenic in CHO cells (Mobay Chemical Corp., 1990).

In vitro tests suggest that metribuzin (Sencor) exposure can result in adduct formation. Using a ^{32}P-postlabeling method, Shah et al. (1997) reported that adducts were formed when metribuzin and its S9-metabolites (1 mM) were reacted with calf thymus DNA for 3.5 hours. The adducts were analyzed using either nuclease P1 or butanol enrichment method. Benzo(a)pyrene was used as the positive control. Compared to the adducts formed in control DNA (5.6 adducts per 10^9 nucleotides), metabolites of metribuzin produced 48.0 total adducts per 10^9 nucleotides, as analyzed by nuclease P1 enrichment method. Analysis of the adducts produced by metribuzin, utilizing the butanol enrichment method, yielded three unique adducts. The major adduct was produced at 281.5 total adducts per 10^9 nucleotides. Adduct formation by metribuzin is less than the adduct formation from benzo(a)pyrene. Benzo(a)pyrene produced 1893 and 1707 adducts per 10^9 nucleotides as analyzed by the nuclease P1 and the butanol enrichment methods, respectively, under similar conditions. Utilizing nuclease P1 and the butanol enrichment methods, Shah et al. reported that, unlike benzo(a)pyrene, the type of adducts formed by metribuzin metabolites were not similar. However, metribuzin (Sencor) did test positive for DNA adduct formation, when using ^{32}P-postlabeling with nuclease P1 enrichment.

Metribuzin exposure produced a negative response in the SOS Chromotest (DNA damage) conducted in *Escherichia coli* with or without metabolic activation (Xu and Schurr,

1990). In a recent study, Venkat et al. (1995) reported mild genotoxic effects of metribuzin using a similar SOS chromotest. The test compounds were tested in 10% dimethylsulfoxide (DMSO) or in micellar solution in sodium taurocholate in order to simulate conditions that are present in the gastrointestinal tract. The activity of the β-galactosidase was 199 and 636 per μmole depending on whether metribuzin was dissolved in DMSO or sodium taurocholate solution, respectively. The genotoxic activity of metribuzin was 26-43 times less than that of the positive control, 4-nitroquinoline oxide (4-NQO). The activity of the β-galactosidase for the positive control (4-NQO) was 8,557 and 16,734 per μmole in DMSO and sodium taurocholate solutions, respectively.

7.3.2 Immunotoxicity

There are no studies available which examine the relationship between metribuzin exposure and immunotoxic effects.

7.3.3 Hormonal Disruption

In vivo metribuzin exposure has been shown to affect the endocrine system. For example, Porter et al. (1993) measured thyroxine and somatotropin levels in rats after exposure to metribuzin. Metribuzin was administered orally in drinking water to Sprague-Dawley rats (n=6; 125-150g) for 6 or 16 weeks. It was observed that the rats treated with metribuzin had hyperthyroidism. Metribuzin exposure (0-10,000 ppm) caused a significant ($p < 0.0005$) increase in the plasma thyroxine levels after 7, 13 or 16 weeks of exposure in both male and female rats. It was determined that somatotropin levels were not affected by metribuzin exposure.

Christenson and Wahle, (1993) reported a statistically significant increase in thyroxine (T4) and decrease in triiodothyronine (T3) levels at all dose levels in Fischer 344 rats receiving 0, 30, 300 or 900 ppm metribuzin (93.0% active ingredient) for 104 weeks.

Flucke and Hartmann (1989) also observed a decrease in triiodothyronine (T3) in male New Zealand rabbits exposed dermally to metribuzin (DIC 1468, technical 94%) at 0, 40, 200, or 1,000 mg/kg-day (6 hours/day; 5 days/week) for 3 weeks.

Kowaski et al. (1986) administered metribuzin (92.6% active ingredient) to pregnant Charles River rats in doses of 0, 25, 70 or 200 mg/kg-day by gavage on gestation days 6-18. The high-dose (200 mg/kg-day) group exhibited a statistically significant increase in thyroid weight. A decrease in T4 levels was observed in both the 70 and 200 mg/kg-day dose groups.

7.3.4 Physiological or Mechanistic Studies

The major toxic effects that result from metribuzin exposure are changes in body weight gain, survival rate, and liver and thyroid function. These effects are mainly systemic and the mode of action has not been investigated. In addition, metribuzin exposure has also been shown to affect hormonal levels such as triiodothyronine, thyroxine, and somatotropin.

7.3.5 Structure-Activity Relationship

There are no studies available which examine the structure-activity relationship of metribuzin.

7.4 Hazard Characterization

7.4.1 Synthesis and Evaluation of Major Non-Cancer Effects

While the studies relating to the metribuzin exposure on human health effects are lacking, the hazard characterization is performed from the available animal studies. Studies conducted in animals suggest that metribuzin exposure causes low acute toxicity as evidenced by the reported high LD_{50} values (Kimmerle et al., 1969; Morgan, 1982; Hartley and Kidd, 1987). Also, acute exposure studies suggest that metribuzin, at the doses tested, does not result in eye or dermal irritations (Kimmerle et al., 1969). Subchronic studies suggest that metribuzin could cause adverse effects in body weight gain, organ weight, and hematological parameters. For example, a significant reduction in body weight gain and an increase in liver and thyroid weights were reported in Wistar rats exposed to metribuzin at 1,500 ppm (Loser et al., 1969). Three weeks of dermal exposure to metribuzin (1,000 mg/kg) in rabbits also resulted in an increase in liver enzymes such as N-demethylase and cytochrome P450 (Flucke and Hartmann, 1989). These effects are not pronounced when the studies were conducted at lower doses in dogs. Three-month metribuzin exposure to Beagle dogs did not affect body weight gain or food consumption, but altered the clinical parameters such as SGOT and SGPT levels (Chaisson and Cueto, 1970).

Chronic effects of metribuzin exposure may include changes in body weight gain, mortality, liver enzyme activities and histopathological changes. Two-year feeding studies were performed on rats (Loser and Mohr, 1974; Christenson and Wahle, 1993), mice (Hayes, 1981) and Beagle dogs (Loser and Mirea, 1974). In general, there were no significant differences in body weight gain, food consumption or mortality after two years of exposure to metribuzin to rats (Loser and Mohr, 1974) and mice (Hayes, 1981). However, Christenson and Wahle (1993) observed a decrease in body weight gain in rats after metribuzin treatment. The differences in body weight gain observed in rats could possibly be attributed to the higher dose (900 ppm) administered by Christenson and Wahle (1993) as compared to a maximum dose of 100 ppm given by Loser and Mohr (1974).

Major histopathological changes reported by one study after chronic feeding of metribuzin include a significant increase in corneal neovascularization, the incidence of a discolored zone in the liver, an enlarged abdomen, enlarged adrenal and thyroid glands, ocular opacity, and enlarged epididymal mass in male rats and the presence of ovarian cysts in female rats (Christenson and Wahle 1993).

Chronic exposure to metribuzin (1,500 ppm) could cause a significant increase in the mortality rate in Beagle dogs. Liver dysfunction was also observed as evidenced by elevation in the activities of liver enzymes such as SGOT, SGPT and OCT. In addition, an increase in thyroid

weight was observed in the high dose group of both males and females (Loser and Mirea, 1974). However, inconsistent hematological results were observed in mice following chronic exposure to metribuzin (Hayes, 1981).

There are a few studies available on metribuzin treatment and developmental and reproductive effects. These studies were performed using rats (Kowaski et al., 1986; Machemer, 1972) and rabbits (Unger and Shellenberger, 1981; Clemens and Hartnagel, 1989). In general, the maternal toxic effects are accompanied by little toxic effect to the fetus. These maternal toxic effects are characterized by a reduction in body weight gain and food consumption. In a two-generation reproduction study, Porter et al. (1988) reported that F_0 and F_1 generations consumed less food and gained less body weight. Necropsy findings in both the F_0 and F_1 generations were not affected by metribuzin exposure. Also, no treatment-related effects were reported in a 3-generation reproduction study in rats (Loser and Siegmund, 1974).

There are no animal studies available which have examined neurotoxic or immunotoxic effects of metribuzin. However, metribuzin exposure could produce some endocrine effects *in vivo*. For example, evidence suggests that metribuzin could elevate plasma thyroxine (T4) levels in rats (Porter et al., 1993; Christenson and Wahle, 1993) and decrease triiodothyronine (T3) levels in rats (Christenson and Wahle, 1993) and rabbits (Flucke and Hartmann, 1989).

A few inhalation studies are available on metribuzin exposure and the effects are comparable to the existing oral exposure studies. An increase in thyroid and liver weights as well as liver enzyme activities such as N-demethylase, O-demethylase and cytochrome P450 was reported in Wistar rats exposed to metribuzin at 720 mg/m^3 (Thyssen, 1981).

7.4.2 Synthesis and Evaluation of Carcinogenic Effects

There are no human studies available which have examined the relationship between exposure to metribuzin and cancer. Metribuzin exposure did not increase the incidence of tumors in a lifetime dietary study using CD-1 mice when compared to both concurrent and historic controls (Hayes, 1981). In a 2-year feeding study utilizing Wistar rats, there were no significant differences in neoplastic findings between the test and control groups (Loser and Mohr, 1974; Christenson and Wahle, 1993). Short-term studies in bacteria and mammalian systems suggest that metribuzin is not mutagenic. Recent *in vitro* studies suggest, however, that metribuzin can induce adduct formation (Shah et al., 1997).

7.4.3 Mode of Action and Implications in Cancer Assessment

The available evidence from animal studies suggest that there is little data to support metribuzin-induced carcinogenicity and therefore no studies are reported which examine the mode of action of metribuzin for cancer effects.

7.4.4 Weight of Evidence Evaluation for Carcinogenicity

There are no studies identified that examine the carcinogenic effects of metribuzin on humans. There are three lifetime studies which have been reported, one in mice and two in rats, that examine the relationship between metribuzin exposure and tumor incidence. Evidence from these animal studies is inadequate and therefore, metribuzin is classified as a class D carcinogen, applying the criteria described in the EPA's guidelines for the assessment of carcinogenic risk (U.S. EPA, 1986).

7.4.5 Sensitive Populations

There are no human studies available which examine the toxic effects of metribuzin and its effect on sensitive populations.

8.0 DOSE-RESPONSE ASSESSMENT

8.1 Dose-Response for Non-Cancer Effects

8.1.1 RfD Determination

Choice of Principal Study

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects. The RfD is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The principal study utilized for RfD derivation, as recommended by the OPP/HED RfD Committee, was the chronic study in rats conducted by Christenson and Wahle (1993) in rats described in section 7.2.6. A 2-year feeding study was conducted in which Fischer 344 rats received 0, 30, 300 or 900 ppm (0, 1.3, 13.8, 42.2 mg/kg-day in males; 0, 1.6, 17.7, 53.6 mg/kg-day females) metribuzin (93.0% active ingredient) for 104 weeks. At 30 ppm (1.3 mg/kg-day for males and 1.6 mg/kg-day for females), both sexes exhibited increased absolute and relative thyroid weights, statistically significant increases in blood levels of thyroxine (T4), and statistically significant decreases in blood levels of triiodothyronine (T3). Females also exhibited decreased lung weight. However, these effects were considered to be of marginal biological significance. Therefore, the RfD Committee determined that the 30 ppm dose (1.3 mg/kg-day in males) should be considered the NOAEL.

RfD Derivation

$$\text{RfD} = \frac{1.3 \text{ mg/kg-day}}{100} = 0.013 \text{ mg/kg-day}$$

Based on a chronic exposure study, an uncertainty factor of 100 was used to account for inter-species extrapolation (10) and intra-species variability (10).

8.1.2 RfC Determination

There is insufficient data available from which to derive the RfC at this time.

8.2 Dose-Response for Cancer Effects

In a study by Hayes (1981), metribuzin was orally administered via the diet to mice (50/sex/dose) at dose levels of 200, 800 or 3,200 ppm (30, 120 or 480 mg/kg-day) for 24 months. Following treatment, the incidence of tumor formation was analyzed in a variety of tissues. Neoplasms of various tissues and organs were similar in type, location, time of occurrence, and incidence in control and treated animals. The mice study is supported by the tumor incidence data observed in 2-year feeding cancer studies in rats (Loser and Mohr, 1974; Christenson and Wahle, 1993).

Applying the criteria described in EPA's guidelines for assessment of carcinogenic risk (U.S. EPA, 1986), metribuzin should be classified in Group D: not classifiable as to human carcinogenicity. This category is used for substances with inadequate animal evidence of carcinogenicity.

9.0 REGULATORY DETERMINATION AND CHARACTERIZATION OF RISK FROM DRINKING WATER

9.1 Regulatory Determination for Chemicals on the CCL

The Safe Drinking Water Act (SDWA), as amended in 1996, required the U.S. Environmental Protection Agency (EPA) to establish a list of contaminants to aid the agency in regulatory priority setting for the drinking water program. EPA published a draft of the first Contaminant Candidate List (CCL) on October 6, 1997 (62 FR 52193, U.S. EPA, 1997). After review of and response to comments, the final CCL was published on March 2, 1998 (63FR 10273, U.S. EPA, 1998). The CCL grouped contaminants into three major categories as follows:

Regulatory Determination Priorities - Chemicals or microbes with adequate data to support a regulatory determination.

Research Priorities - Chemicals or microbes requiring research for health effects, analytical methods, and/or treatment technologies.

Occurrence Priorities - Chemicals or microbes requiring additional data on occurrence in drinking water.

The March 2, 1998 CCL included one microbe and 19 chemicals in the regulatory determination priority category. More detailed assessments of the completeness of the health, treatment, occurrence and analytical method data led to a subsequent reduction of the regulatory determination priority chemicals to a list of 12 (one microbe and 11 chemicals) which was distributed to stakeholders in November 1999.

SDWA requires EPA to make regulatory determinations for no fewer than five contaminants in the regulatory determination priority category by August, 2001. In cases where the Agency determines that a regulation is necessary, the Agency has two years to propose an NPDWR and one and a half years to finalize the rule. The Agency is given the freedom to also determine that there is no need for a regulation if a chemical on the CCL fails to meet the statutory criteria established by SDWA and described in section 9.1.1.

9.1.1 Criteria for Regulatory Determination

These are the three criteria used to determine whether or not to regulate a chemical on the CCL:

The contaminant may have an adverse effect on the health of persons

The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern

In the sole judgment of the administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

The findings for all three criteria are used in making a determination to regulate a contaminant. As required by SDWA, a decision to regulate commits the EPA to publication of a Maximum Contaminant Level Goal (MCLG) and promulgation of a National Primary Drinking Water Regulation (NPDWR) for that contaminant. The Agency may determine that there is no need for a regulation when a contaminant fails to meet one of the criteria. A decision not to regulate is considered a final Agency action and is subject to judicial review. The Agency can choose to publish a Health Advisory (a nonregulatory action) or other guidance for any contaminant on the CCL, independent of the regulatory determination.

9.1.2 National Drinking Water Advisory Council Recommendations

In March 2000, the U.S EPA convened a Working Group under the National Drinking Water Advisory Council (NDWAC) to help develop an approach for making regulatory determinations. The Working Group developed a protocol for analyzing and presenting the available scientific data and recommended methods to identify and document the rationale supporting a regulatory determination decision. The NDWAC Working Group report was presented to and accepted by the entire NDWAC in July 2000.

Because of the intrinsic difference between microbial and chemical contaminants, the Working Group developed separate but similar protocols for microorganisms and chemicals. The approach for chemicals was based on an assessment of the impact of acute, chronic, and lifetime exposures, as well as a risk assessment that includes evaluation of occurrence, fate, and dose-response. The NDWAC Protocol for chemicals is a semi-quantitative tool for addressing each of the three CCL criteria. The NDWAC requested that the Agency use good judgement in balancing the many factors that need to be considered in making a regulatory determination. The U.S. EPA modified the semi-quantitative NDWAC suggestions for evaluating chemicals against the regulatory determination criteria and applied them in decision making. The quantitative and qualitative factors for metribuzin that were considered for each of the three criteria are presented in the sections that follow.

9.2 Health Effects

The first criterion asks if the contaminant may have an adverse effect on the health of persons. Because all chemicals have adverse effects at some level of exposure, the challenge is to define the dose at which adverse health effects are likely to occur, and to estimate a dose at which adverse health effects are either not likely to occur (threshold toxicant), or have a low probability for occurrence (non-threshold toxicant). The key elements that must be considered in evaluating the first criterion are the mode of action, the critical effect(s), the dose-response for critical effect(s), the RfD for threshold effects, and the slope factor for non-threshold effects.

A full description of the health effects associated with exposure to metribuzin is presented in Chapter 7 of this document and summarized below in Section 9.2.2. Chapter 8 and Section 9.2.3 present dose-response information.

9.2.1 Health Criterion Conclusion

Although there are no studies reporting the adverse effects of metribuzin on human health, animal studies indicate that metribuzin has the potential to cause adverse health effects at high doses. Exposure to metribuzin may occur primarily in an occupational setting, particularly in the agriculture industry where it is used as an herbicide. The RfD of 0.013 mg/kg-day was derived from a study reporting the adverse health effects of metribuzin in rats.

9.2.2 Hazard Characterization and Mode of Action Implications

There are no epidemiology studies that have assessed adverse human health effects caused by exposure to metribuzin. Acute toxicity animal studies indicate that metribuzin induces low toxicity as evidenced by the relatively high LD_{50} values (Kimmerle et al., 1969; Morgan, 1982; Hartley and Kidd, 1987). In addition, metribuzin has not been found to cause eye irritation in rabbits, and causes only slight dermal irritation in rabbits (Kimmerle et al., 1969).

Subchronic studies in animals suggest that metribuzin may cause adverse effects on body weight gain, organ weight and hematological parameters. Wistar rats exposed to metribuzin in the diet at 1500 ppm for three months exhibited a significant reduction in body weight gain, and increased liver and thyroid weights (Loser et al., 1969). However a 3-month dietary exposure in Beagle dogs did not affect body weight gain or food consumption, and only altered clinical parameters such as SGOT and SGPT levels (Chaisson and Cueto, 1970).

Chronic studies of metribuzin report effects on body weight gain, mortality, liver enzyme activities and histopathological changes. Two-year feeding studies conducted in rats (0, 25, 35, 100 or 300 ppm) and mice (0, 200, 800 or 3200 ppm) indicated no significant differences in body weight gain, food consumption, or mortality (Loser and Mohr, 1974; Hayes, 1981). Another two-year feeding study in rats using a higher dose (900 ppm) of metribuzin did report a decrease in body weight gain (Christenson and Wahle, 1993). This study also reported histopathological changes such as significant increases in corneal neovascularization, discolored zones in the liver, an enlarged abdomen, enlarged adrenal and thyroid glands, ocular opacity, an enlarged epididymal mass in males, and the presence of ovarian cysts in female rats (Christenson and Wahle, 1993). In Beagle dogs, chronic exposure to the highest dose of 1,500 ppm caused a significant increase in the mortality rate and liver dysfunction as evidenced by increases in the activity of liver enzymes such as SGOT, SGPT and OCT (Loser and Mirea, 1974). Thyroid weight was also increased in the highest dose group. Histopathologic findings included liver and kidney damage at the highest dose. The liver and kidney effects, decreased body weight gain, and mortality at the highest dose are considered the critical effects of metribuzin exposure.

There are few studies that have assessed the developmental and reproductive effects of metribuzin exposure. In general, maternal toxicity effects observed in rats and rabbits include reduced body weight gain and food consumption, and are accompanied by slight toxicity to the fetus (Kowaski et al., 1986; Machemer, 1972; Unger and Shellenberger, 1981; Clemens and Hartnagel, 1989). A two-generation study in rats reported that both F_0 and F_1 generations consumed less food and gained less body weight (Porter et al., 1988). Necropsy findings in both generations were not affected by exposure to metribuzin. Another 3-generation reproduction study in rats found no treatment-related effects (Loser and Siegmund, 1974).

No animal studies have addressed the neurologic or immunotoxic effects of metribuzin. There is evidence of endocrine effects induced by metribuzin, including elevated plasma thyroxine levels in rats and decreased triiodothyronine levels in rats and rabbits (Porter et al. 1993; Christenson and Wahle, 1993; Flucke and Hartmann, 1989).

The EPA has classified metribuzin as a class D carcinogen due to inadequate carcinogenicity data in humans and animals. A lifetime dietary study in CD-1 mice and 2-year feeding studies in Wistar rats were negative for the induction of tumors compared to control incidences (Hayes, 1981; Loser and Mohr, 1974; Christenson and Wahle, 1993).

9.2.3 Dose-Response Characterization and Implications in Risk Assessment

The principal study utilized for RfD derivation, as recommended by the OPP/HED RfD Committee, was the chronic study in rats conducted by Christenson and Wahle (1993) in rats described in section 7.2.6. A 2-year feeding study was conducted in which Fischer 344 rats received 0, 30, 300 or 900 ppm (0, 1.3, 13.8, 42.2 mg/kg-day in males; 0, 1.6, 17.7, 53.6 mg/kg-day females) metribuzin (93.0% active ingredient) for 104 weeks. At 30 ppm (1.3 mg/kg-day for males and 1.6 mg/kg-day for females), both sexes exhibited increased absolute and relative thyroid weights, statistically significant increases in blood levels of thyroxine (T4), and statistically significant decreases in blood levels of triiodothyronine (T3). Females also exhibited decreased lung weight. However, these effects were considered to be of marginal biological significance. Therefore, the RfD Committee determined that the 30 ppm dose (1.3 mg/kg-day in males) should be considered the NOAEL. The RfD of 0.013 mg/kg-day was derived by dividing the NOAEL by an uncertainty factor of 100, which was used to account for inter- and intra-species variability.

9.3 Occurrence in Public Water Systems

The second criterion asks if the contaminant is known to occur or if there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern. In order to address this question, the following information was considered:

- Monitoring data from public water systems
- Ambient water concentrations and releases to the environment
- Environmental Fate

Data on the occurrence of metribuzin in public drinking water systems were the most important determinants in evaluating the second criterion. EPA looked at the total number of systems that reported detections of metribuzin, as well as those that reported concentrations of metribuzin above an estimated drinking water health reference level (HRL). For noncarcinogens the estimated HRL risk level was calculated from the RfD assuming that 20% of the total exposure would come from drinking water. For carcinogens, the HRL was the 10^{-6} risk level. The HRLs are benchmark values that were used in evaluating the occurrence data while the risk assessments for the contaminants were being developed.

The available monitoring data, including indications of whether or not the contamination is a national or a regional problem, are included in Chapter 4 of this document and are summarized below. Additional information on production, use, and environmental fate are found in Chapters 2 and 3.

9.3.1 Occurrence Criterion Conclusion

The available data on metribuzin production and use indicate a modestly declining trend. Although detection of metribuzin is found in both surface and ground waters of urban and agricultural regions, concentrations are extremely low and well below the HRL or half the HRL. In regards to drinking water, metribuzin detection frequencies and concentrations are extremely low to undetectable, with the exception of detections in Pennsylvania, Indiana, Illinois and Washington. These data indicate that although metribuzin is found in ambient waters, little to no metribuzin is detected in drinking water systems.

9.3.2 Monitoring Data

Drinking Water

A national cross-section of 20 states reported metribuzin detection data in the SDWIS/FED database. This cross-section provides a good representation of the nation's varied climatic and hydrogeologic regions, and the breadth of pollution potential. In addition, occurrence data is presented from all the states participating under the Unregulated Contaminant Monitoring (UCM) program begun in 1991. Metribuzin was not included in this program until Round 2, which began in 1993.

In the cross-section of 20 states, approximately 0.007% of Public Water Systems (PWS) reported detections of metribuzin above the minimum reporting level (MRL), affecting about 0.0003% of the population. Only the state of Washington reported a metribuzin detection above the MRL, at a level of 0.10 µg/L, which is far below the Health Reference Level (HRL) of 91 µg/L. A national extrapolation of this data indicates that approximately 5 PWSs would experience detections of metribuzin above the MRL, and that approximately 1,000 people would be affected.

When all the states participating in Round 2 of the UCM program were considered, 0.28% of PWSs experienced detections above the MRL. This indicates that approximately 1.61% of the population, or 3.4 million people nationally, is affected by concentrations of metribuzin above the MRL. No PWSs experienced detections > ½ HRL or > HRL. Therefore, 0% of the population is affected by metribuzin concentrations > ½ HRL or > HRL. The median and 99th percentile concentrations of detections are 1.0 µg/L and 3 µg/L, respectively.

Ambient Water

The USGS began the National Ambient Water Quality Assessment (NAWQA) program in 1991 to monitor water quality status and trends in the U.S. This program consists of 59 watersheds and aquifers referred to as "study units" and represents approximately two-thirds of the overall water usage and a similar proportion of the population served by public water systems. The Method Detection Limit (MDL) for metribuzin is 0.004 µg/L.

Detection frequencies and concentrations of metribuzin in ambient surface and ground waters are low. Surface waters exhibited the highest maximum concentration of metribuzin at 0.530 µg/L, with a reported frequency of 13.82% of samples with concentrations greater than the MDL. Although the occurrence in ground water is lower than in surface water, detection in 1.95% of ground water samples at a maximum concentration of 0.300 µg/L make metribuzin one of the 21 most commonly detected pesticides in intensive NAWQA monitoring. In both surface and ground waters, metribuzin was more frequently detected in agricultural regions as compared to urban areas.

9.3.3 Use and Fate Data

Metribuzin, a synthetic organic compound, is a selective triazinone herbicide used to discourage growth of broadleaf weeds and annual grasses among vegetable crops and turf grass. Using data from the USDA and NCFAP, the EPA estimates that the average annual use for the years 1990-94 at 2.8 million pounds of active ingredient with 8.5 million acres treated. The USGS estimates that 2.7 million pounds of metribuzin treating 8.4 million acres were used in 1992. The non-agricultural use of metribuzin is minimal. Table 3-1 of Chapter 3 indicates a modest decline of metribuzin use from 1990-1999.

Data from the Toxic Release Inventory (TRI) indicate a general decline in environmental releases of metribuzin between 1995 and 1998 (Table 3-2). Air emissions are reported to have declined although surface water discharges have increased.

Metribuzin is a solid at ambient temperatures and has a low vapor pressure. Therefore, it is unlikely to readily partition to air. Since metribuzin is not labeled for residential use, it is not anticipated to be found in residential soils. The Organic Carbon Partition Coefficient (K_{oc}) is 95, and indicates that metribuzin is highly mobile in soil. It is also moderately adsorbed on soils with high clay or organic content and leaches more readily from sandy soils. In soil, biodegradation is the primary fate process (HSDB, 2000). In the aquatic environment, volatilization from water

and bioconcentration in fish are not anticipated to be relevant (HSDB, 2000). No data are available for the biodegradation of metribuzin in water.

9.4 Risk Reduction

The third criterion asks if, in the sole judgement of the Administrator, regulation presents a meaningful opportunity for health risk reduction for persons served by public water systems. In evaluating this criterion, EPA looked at the total exposed population, as well as the population exposed above the estimated HRL. Estimates of the populations exposed and the levels to which they were exposed were derived from the monitoring results. These estimates are included in Chapter 4 of this document and summarized in Section 9.4.2 below.

In order to evaluate risk from exposure through drinking water, EPA considered the net environmental exposure in comparison to the exposure through drinking water. For example, if exposure to a contaminant occurs primarily through ambient air, regulation of emissions to air provides a more meaningful opportunity for EPA to reduce risk than regulation of the contaminant in drinking water. In making the regulatory determination, the available information on exposure through drinking water (Chapter 4) and information on exposure through other media (Chapter 5) were used to estimate the fraction that drinking water contributes to the total exposure. The EPA also evaluated effects on potentially sensitive populations, including fetuses, infants and children. The sensitive population considerations are included in Section 9.4.4.

9.4.1 Risk Criterion Conclusion

Based on the data from the cross-section analysis of 20 states, metribuzin exposure from drinking water would be very low with only 1,000 people exposed nationally. When all the Round 2 data are considered, including data from the state of Pennsylvania, approximately 3.4 million people nationally are exposed to any concentration of metribuzin. Aside from the potential of occupational exposure, no other source of exposure would lead to significant doses of metribuzin. These observations indicate that regulation of metribuzin in drinking water would have little impact on human risk reduction.

9.4.2 Exposed Population Estimates

As described in 9.3.1, a cross-section survey of 20 states reported that 0.007% of Public Water Systems had detections of metribuzin above the minimum reporting level (MRL), affecting less than 0.0003% of the population. A national extrapolation of this data indicates that approximately 1,000 people would be exposed to metribuzin through the drinking water. Of the 20 states in this cross-section survey, only the state of Washington reported a detection of metribuzin. Since Washington is the only state to report a metribuzin detection at 0.10 µg/L, this value is both the median and 99th percentile concentrations.

However, when all of the participating states in Round 2 of the UCM program were considered, 0.28% of PWSs reported detections above the MRL. National extrapolation of this

data indicates that approximately 1.6% of the population, or 3.4 million people, are exposed to concentrations above the MRL.

9.4.3 Relative Source Contribution

Relative source contribution analysis compared the magnitude of exposure to metribuzin expected via drinking water and the magnitude of exposure from other media, such as food, air and soil. The intake of metribuzin from drinking water can be calculated from the median concentrations described above for both the cross-section study and the study of all the Round 2 states. Using the median metribuzin level from the 20 state cross-section study of 0.10 µg/L, an average daily intake of 2 L/day for an adult, and an average weight of 70 kg for an adult, the corresponding dose would be 2.8×10^{-3} mg/kg-day for adults. For children, assuming an intake of 1 L/day and an average weight of 10 kg, the dose would be 1.0×10^{-2} mg/kg-day.

As part of the FDA's Regulatory Monitoring Program, 9,438 domestic and imported food samples were analyzed for pesticides, including metribuzin. Metribuzin was not detected in any samples of grains, milk products, fruits or vegetables. In addition, no detections were found in 218 domestic and 298 imported fish and shellfish samples. The daily intake of metribuzin from food is anticipated to be close to zero.

No data are available for the ambient levels of metribuzin in air. However, metribuzin is a solid at ambient temperatures and has a low vapor pressure; partitioning of metribuzin into air is highly unlikely. Therefore, the average daily intake for the general population is anticipated to be close to zero. However, inhalation of metribuzin may be potentially significant for occupational exposure. The occupational subgroup may include workers involved in the mixing, loading, handling and application of metribuzin. The EPA has estimated that inhalation exposures of this subgroup range from 0.006 to 91.14 mg/day. Calculations of doses based on this range of exposure and 70 kg body weight are 8.6×10^{-5} to 1.3 mg/kg-day.

Metribuzin is not labeled for residential use and so it is not anticipated to be found in residential soils. General population exposures are anticipated to be close to zero. In agricultural regions where metribuzin is applied, metribuzin may be found in soils in concentrations as high as 0.78 mg/kg. Based on an average body weight of 70 kg and a daily soil intake of 480 mg/day, the maximum daily intake for a contact intensive worker would be 5.3×10^{-3} mg/kg-day, which is below the RfD.

For estimating the HRL from the RfD, the default value of 20% was used for the relative source contribution assuming that the total exposure to metribuzin is from drinking water.

9.4.4 Sensitive Populations

No sensitive populations to metribuzin have been identified.

9.5 Regulatory Determination Summary

Although there is evidence from animal studies that metribuzin may cause adverse health effects at high doses, its occurrence in public water systems and the numbers of people potentially exposed through drinking water are low. In addition, there are no available studies, either epidemiological or case-studies of accidentally exposed agricultural workers, assessing adverse health effects in humans due to metribuzin. Overall, metribuzin is not anticipated to cause adverse health effects in humans at the concentrations detected in public water systems and is unlikely to expose a large number of people outside of an occupational setting. For these reasons, EPA may not propose to regulate metribuzin with NPDWR. All final determinations and future analysis will be presented in the Federal Register Notice covering CCL proposals

10.0 REFERENCES

ACGIH. 1986. Documentation of the threshold limit values and biological exposure indices, 5th ed, Cincinnati, OH. American Conference of Governmental Industrial Hygienists, Inc. 6:1042, 1991. (as cited in RTECS, 2000; HSDB, 2000).

Barbash, J. E. and E. A. Resek. 1996. Pesticides in Ground Water: Distribution, trends, and governing factors. Volume two of Pesticides in the Hydrologic System. Chelsea, MI: Ann Arbor Press, Inc. 588 pp.

Bouchard, D.C., T.L. Lavy, and D.B. Marx. 1982. Fate of metribuzin, metolachlor and fluometuron in soil. Weed Science 30:629-632.

Brown, D.F., D.K. McCool, R.I. Papendick, et al. 1985. Herbicide residues from winter wheat triticum-aestivum plots effect of tillage and crop management. Journal of Environmental Quality. 14 (4):521-532.

Burgard, D.J., R.H. Dowdy, W.C. Koskinen, et al. 1994. Movement of metribuzin in a loamy sand soil under irrigated potato production. Weed Science 42 (3):446-452.

Cadmus. 2000. Methods for Estimating Contaminant Occurrence and Exposure in Public Drinking Water Systems in Support of CCL Determinations. Draft report submitted to EPA for review July 25, 2000.

Cadmus. 2001. Occurrence estimation methodology and occurrence findings report for six-year regulatory review. Draft report to U.S. EPA for review October 5, 2001.

Cain, K., C. Hanlon and J. Lane. 1987. The excretion and metabolism of Sencor by rats. Unpublished study. Submitted by Mobay Chemical Corp. Kansas City, MO (MRID 40255503) (as cited in U.S. EPA 1998).

Cessna, A.J. 1998. Metribuzin residues in lentil following postemergence application. Canadian Journal of Plant Science 78(1):167-169.

Chaisson, C.F. and C. Cueto. 1970. 90-day subacute oral toxicity study of BAY 94337 in Beagle dogs. Submitted by Mobay Chemical Corp. Kansas City, MO (MRID 00106162)

Christenson, W.R. and B.S. Wahle. 1993. Technical Grade Metribuzin (Sencor®): A combined chronic toxicity/oncogenicity feeding toxicity study in the rat. Unpublished study. Prepared by Miles Inc. (MRID 42672501)

Clemens, G., and R. Hartnagel Jr. 1989. Teratology study in the rabbit with Sencor Technical (Metribuzin). A Unpublished study. Prepared by Miles Inc. (MRID 41249201)

Cohen, B., R. Wiles, and E. Bondoc. 1995. Weed Killers by the Glass: a citizen's tap water monitoring project in 29 cities. Washington, D.C.: Environmental Working Group. 83 pp.

Crawford, C. and R. Anderson. 1972. The acute dermal toxicity of Sencor Technical and Sencor 50% wettable powder to rats and rabbits: Report No. 33123. Unpublished study. Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00106149) (as cited in U.S. EPA, 1998a)

Crawford, C.R. and R. H. Anderson*. 1974. The acute oral toxicity of Sencor technical, several Sencor metabolites and impurities to rats and guinea pigs. Report no. 38927. Rev. unpublished study. MRID 00045270 (as cited in U.S. EPA1988)

Dao, T.H. 1995. Subsurface mobility of metribuzin as affected by crop residue placement and tillage method. Journal of Environmental Quality 24:1193-1198.

EXTOXNET. 1998. Pesticide Information Profile: Metribuzin. Ithaca, NY: Extension Toxicology Network, Pesticide Management Education Program. Available on the Internet at http://pmep.cce.cornell.edu/profiles/extoxnet/metiram-propoxur/metribuzin-ext.html#top Last modified 03/11/1998.

Flucke, W. and E. Hartmann. 1989. DIC 1468. Technical grade: (Common Name:Metribuzin): Subacute dermal toxicity study in rabbits. Unpublished study. Prepared by Bayer. (MRID 43970701) (as cited in U.S. EPA 1998)

Gallaher, K. and T.C. Mueller. 1996. Effect of crop presence on persistence of atrazine, metribuzin, and clomazone in surface soil. Weed Science 44 (3):698-703.

Gilliom, R.J., D.K. Mueller, and L.H. Nowell. In press. Methods for comparing water-quality conditions among National Water-Quality Assessment Study Units, 1992-95. U.S. Geological Survey Open-File Report 97-589.

Hallberg, G.R. 1989. Pesticide pollution of groundwater in the humid United States. Agriculture, Ecosystems and Environment. v. 26, pp. 299-367.

Hallberg, G.R., D.G. Riley, J.R. Kantamneni, P. J. Weyer, and R.D. Kelley. 1996. *Assessment of Iowa Safe Drinking Water Act Monitoring Data: 1988-1995*. Research Report No. 97-1. Iowa City: The University of Iowa Hygienic Laboratory. 132 pp.

Hargroder, T.G. and R.L. Rogers. 1974. Behavior and fate of metribuzin in soybean and hemp sesbania. Weed Science 22(3): 238-245.

Hartley,D. And H. Kidd (eds). 1987. The agrochemicals handbook. 2nd ed. Lechworth, Herts, England: The Royal Society of Chemistry, pp. A280 (as cited in HSDB, 2000).

Hayes, R.H. 1981. Metribuzin (Sencor®) oncogenicity study in mice. Unpublished study. Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00087795)

HSDB. 2000. Metribuzin (CASRN: 21087-64-9). HSDB #6844. http://toxnet.nlm.nih.gov/

Kimmerle, G., B. Solecke, and D. Lorke. 1969. Bay 94337. Toxicological studies from Dr. George Kimmerle and Dr. Brigitte Solecke: Report No. 1574; 25942. Unpublished study. Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00106158) (as cited in U.S. EPA, 1998a)

Kolpin, D. W., M. R. Burkart, and E. M. Thurman. 1994. Herbicides and Nitrate in Near-Surface Aquifers in the Midcontinental United States, 1991. U.S. Geological Survey Water-Supply Paper 2413. 34 pp.

Kolpin, D.W., K. E. Zichelle, and E. M. Thurman. 1996. Water Quality Data for Nutrients, Pesticides, and Volatile Organic Compounds in Near-Surface Aquifers of the Midcontinental United States, 1992-94. U.S. Geological Survey Open-File Report 96-435. Prepared in cooperation with the United States Environmental Protection Agency. 47 pp.

Kolpin, D. W., J. E. Barbash, and R. J. Gilliom. 1998. Occurrence of pesticides in shallow groundwater of the United States: initial results from the National Water Quality Assessment Program. Environmental Science & Technology. v. 32, pp. 558-566.

Kowaski, R.L., G.R. Clemens, J. J. Bare and R.E. Hartnagel, Jr. 1986. A teratology study with Sencor Technical (Metribuzin) in the rat: 91330. Unpublished study. Prepared by Miles Laboratories, Inc. (MRID 00163802)

Kross, B.C., G.R. Hallberg, D.R. Bruner, R.D. Libra, K.D. Rex, L.M.B. Weih, M.E. Vermace, L.F. Burmeister, N.H. Hall, K.L. Cherryholmes, J.K. Johnson, M.I. Selim, B.K. Nations, L.S. Seigley, D.J. Quade, A.G. Dudler, K.D. Sesker, M.A. Culp, C.F. Lynch, H.F. Nicholson, and J.P. Hughes. 1990. The Iowa State-Wide Rural Well-Water Survey Water-Quality Data: Initial Analysis. Technical Information Series 19. 142 pp.

Larson, S. J., P. D. Capel, and M.S. Majewski. 1997. Pesticides in Surface Waters: Distribution, trends, and governing factors. Volume three of Pesticides in the Hydrologic System. Chelsea, MI: Ann Arbor Press, Inc. 373 pp.

Larson, S.J., R.J. Gilliom, and P.D. Capel. 1999. *Pesticides in Streams of the United States--Initial Results from the National Water-Quality Assessment Program.* U.S. Geological Survey Water-Resources Investigations Report 98-4222. 92 pp. Available on the Internet at: URL: http://water.wr.usgs.gov/pnsp/rep/wrir984222/

Leahy, P.P., and T.H. Thompson. 1994. *The National Water-Quality Assessment Program.* U.S. Geological Survey Open-File Report 94-70. 4 pp. Available on the Internet at: http://water.usgs.gov/nawqa/NAWQA.OFR94-70.html Last updated August 23, 2000.

Lehman, W.J., W. F. Reehl and D.H. Rosenblatt. 1959. Handbook of chemical property estimation methods. New York: McGraw Hill. (As cited in U.S. EPA 1988)

Lindberg, D. and W. Richter*. 1970. Report to Chemagro Corporation: 90-day subacute oral toxicity of Bay 94337 in beagle dogs: IBT no. C776; 26488. Unpublished study. MRID 00106162. (As cited in U.S. EPA 1988)

Loser, E. and D. Mirea*. 1974. Bay 94337: Chronic toxicity studies on dogs (Two-year feeding experiment): Report No. 4887; Report No. 41814. Unpublished study. submitted by Mobay Chemical Corp., Kansas City, MO. (MRID 00061260)

Loser, E. and U. Mohr*. 1974. Bay 94337: Chronic toxicity studies on rats (Two-year feeding experiment): Report No. 4888; Report No. 41816.Unpublished study. submitted by Mobay Chemical Corp., Kansas City, MO. (MRID 00061261)

Loser, E., L.E. Mawdesley-Thomas and D. Lorke*. 1969. Bay 94337. Subchronic toxicological studies on rats (three-month feeding experiment). Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00106161).

Loser, E. and F. Siegmund*. 1974. Bay 94337. Multigeneration study on rats: Report no. 4889; Report No. 41818. Unpublished study. (MRID 00061262) (As cited in U.S. EPA 1988).

Machemer, L*. 1972. Sencor (Bay 94 337) Studies for possible embryotoxic and teratogenic effects on rats after oral administration (Bay Report No. 3678). Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00061257).

Mathew, R., S. Kacew and S.U. Khan. 1998. Bioavailability in rats of bound pesticide residues from tolerant or susceptible varieties of soybean and canola treated with metribuzin or atrazine. Chemosphere. 36:589-596.

Mobay Chemical Corporation*. 1974a. MRID No. 00086766 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1974b. MRID No. 00086765 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1975. MRID No. 00086767 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation*. 1976. MRID No. 00086768 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1977. MRID No. 00086770 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation*. 1978a. Supplement to synopsis of human safety of Sencor: Supplement no. 3. Summary of studies 235396-3 through 235396-E. Unpublished study. MRID No. 00078084 (as cited in U.S. EPA, 1988)

Mobay Chemical Corporation*. 1978b. MRID No. 00109254 (as cited in U.S. EPA, 1993)
Mobay Chemical Corporation. 1986a. MRID No. 00157526 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1986b. MRID No. 00157527 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1987. MRID No. 40347701 (as cited in U.S. EPA, 1993)

Mobay Chemical Corporation. 1990. MRID No. 41555102 (as cited in U.S. EPA, 1993)

Morgan, D.P. 1982. Recognition and management of pesticide poisonings. EPA 540/9-80-005 (as cited in HSDB, 2000)

Nicholls et al. 1982. Measurement and simulation of the movement and degradation of atrazine and metribuzin in a fallow soil. Pestic. Sci. 12:484-494 (as cited in Burgard, 1994).

PCBPBS. 1984. Pesticide Biochemistry and Physiology. (Academic press, Inc). Vol. 1, 1971, 23: 123 (as cited in RTECS, 2000)

Porter, M.C, V. Jasty, and R.E. Hartnagel Jr. 1988. A two-generation reproduction study in rats with Sencor Technical (Metribuzin). Report No. 98295: Unpublished study. Prepared by Miles Inc. (MRID 40838401)

Porter, W.P., S.M. Green, N.L. Debbink and I. Carlson. 1993. Groundwater pesticides: interactive effects of low concentrations of carbamates, aldicarb and methomyl and the triazine metribuzin on thyroxine and somatotropin levels in white rats. Journal of Toxicology and Environmental Health 40:15-34

RTECS, 2000. http://www.ccohs.ca/products/databases/rtecs.html

Shah, R.G., J. Lagueux, S. Kapur, P. Levallois, P. Ayotte, M. Tremblay, J. Zee and G.G. Poirier. 1997. Determination of genotoxicity of the metabolites of the pesticides Guthion, Sencor, Lorox, Reglone, Daconil, and Admire by ^{32}P-postlabeling. Molecular and Cellular Biochemistry 169; 177-184.

Sharom, M.S. and G.R. Stephenson. 1976. Behavior and fate of metribuzin in eight Ontario soils. Weed Sci. 24:153-160 (as cited in Bouchard et al., 1982).

Shiotsuka, R. 1986. Acute inhalation toxicity study with metribuzin (Sencor) in rats: Study No. 85-041-18: Unpublished study. Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00157524) (as cited in U.S. EPA, 1998a)

Thelin, Gail P., and Leonard P. Gianessi. 2000. Method for Estimating Pesticide Use for County Areas of the Conterminous United States. U.S. Geological Survey Open-File Report 00-250. 62 pp. Available on the Internet at: http://water.wr.usgs.gov/pnsp/rep/ofr00250/ofr00250.pdf

Thyssen J. 1981. DIC 1468: (Sencor Active Ingredient): Subacute inhalation studies with rats: Report No. 9679. Unpublished study. Prepared by Bayer AG, Institute of Toxicology, pp.126 (MRID 00153706) (as cited in U.S. EPA, 1998a)

Unger, T.M. and T.E. Shellenberger*. 1981. A teratological evaluation of Sencor® in mated female rabbits. Final report. Unpublished study. Submitted by Mobay Chemical Corp., Kansas City, MO (MRID 00087796)

USDA. 1997. Agricultural Resources and Environmental Indicators, 1996-97. Agricultural Handbook No. 712. Washington, DC: U.S. Department of Agriculture, Economic Research Service, Natural Resources and Environment Division. 347 pp.

USDA. 2000. Agricultural Chemical Usage (PCU-BB). Available on the Internet at: http://usda.mannlib.cornell.edu/reports/nassr/other/pcu-bb/

U.S. EPA. 1986. U.S. Environmental Protection Agency. Guidelines for carcinogen risk assessment. Fed. Reg. 51 (185):33992-34003. September 24 (as cited in U.S. EPA 1996).

U.S. EPA. 1987. National Primary Drinking Water Regulations-Synthetic Organic Chemicals; Monitoring for Unregulated Contaminants; Final Rule. July 8. Federal Register. vol. 52, no. 130. [52 FR 25720].

U.S. EPA. 1988. Metribuzin. Health Advisories for 50 pesticides. Office of Drinking Water. NTIS No: PB88-245931.

U.S. EPA. 1990. National Survey of Pesticides in Drinking Water Wells. EPA Report 570/9-90-015. Office of Water. 98 pp. + appendices.

U.S. EPA. 1991. National Primary Drinking Water Regulations - Synthetic Organic Chemicals and Inorganic Chemicals; Monitoring for Unregulated Contaminants; National Primary Drinking Water Regulations Implementation; National Secondary Drinking Water Regulations; Final Rule. January 30. Federal Register. vol. 56, no. 20, 3526 - 3597 pp. [56 FR 3526]

U.S. EPA. 1992. Drinking Water; National Primary Drinking Water Regulations – Synthetic Organic Chemicals and Inorganic Chemicals; National Primary Drinking Water Regulations Implementation. July 17. Federal Register. vol. 57, no. 138, 31776 - 31849 pp. [57 FR 31776]

U.S. EPA. 1993. IRIS document for metribuzin.

U.S. EPA. 1996. Emergency Planning and Community Right-to-Know Section 313, List of Toxic Chemicals. Available on the Internet at: http://www.epa.gov/tri/chemls2.pdf. Last modified March 23, 2000. Link to site at: http://www.epa.gov/tri/chemical.htm

U.S. EPA. 1997. Exposure Factor Handbook Volume 1. Office of Research and Development. Washington, D.C. EPA/600/P-95/002Fa.

U.S. EPA. 1997. U.S. Environmental Protection Agency. Announcement of the Draft Drinking Water Contaminant Candidate List; Notice. Fed. Reg. 62(193):52193. October 6.

U.S. EPA. 1998. U.S. Environmental Protection Agency. Announcement of the Drinking Water Contaminant Candidate List; Final Rule. Fed. Reg. 63(274):10273. March 2.

U.S. EPA. 1998a. Registration Eligibility Decision (RED): Metribuzin. EPA Report/738-R-97-006. Washington, DC: Office of Prevention, Pesticides, and Toxic Substances. 215 pp. Available on the Internet at: http://www.epa.gov/oppsrrd1/REDs/ Last modified: 8/29/2000.

U.S. EPA. 1998b. R.E.D. Facts: Metribuzin. EPA Report/738-F-96-006. Washington, DC: Office of Prevention, Pesticides, and Toxic Substances. 7 pp. Available on the Internet at: http://www.epa.gov/oppsrrd1/REDs/ Last modified: 8/29/2000.

U.S. EPA. 1999. A Review of Contaminant Occurrence in Public Water Systems. EPA Report/816-R-99/006. Office of Water. 78 pp.

U.S. EPA. 2000a. TRI Explorer: Are Year-to-Year Changes Comparable? Available on the internet at: www.epa.gov/triexplorer/yearsum.htm Last modified May 5, 2000.

U.S. EPA. 2000b. TRI Explorer: Trends. Available on the internet at: http://www.epa.gov/triexplorer/trends.htm Last modified May 5, 2000.

U.S. EPA. 2000c. The Toxic Release Inventory (TRI) and Factors to Consider when Using TRI Data. Available on the internet at: http://www.epa.gov/tri/tri98/98over.pdf. Last modified August 11, 2000. Link to site at: http://www.epa.gov/tri/tri98

U.S. EPA. 2000d. What is the Toxic Release Inventory. Available on the internet at: http://www.epa.gov/tri/general.htm Last modified February 28, 2000.

U.S. EPA. 2000e. Water Industry Baseline Handbook, Second Edition (Draft). March 17, 2000.

U.S. EPA. 2001a. *Analysis of national occurrence of the 1998 Contaminant Candidate List (CCL) regulatory determination priority contaminants in public water systems*. Office of Water. EPA report 815-D-01-002. 77 pp and appendices.

U.S. EPA. 2001b. *Occurrence of unregulated contaminants in public water systems: An initial assessment.* Office of Water. EPA report 815-P-00-001. Office of Water. 50 pp.

US FDA. 1999. Food and Drug Administration Pesticide Program Residue Monitoring 1999. http://vm.cfsan.fda.gov/~dms/pesrpts.html

USGS. 1998a. Sources & Limitations of Data Used to Produce Maps of Annual Pesticide Use. Available on the Internet at: http://water.wr.usgs.gov/pnsp/use92/mapex.html Last modified 3/20/1998.

USGS. 1998b. Annual Use Maps. Available on the Internet at: http://water.wr.usgs.gov/pnsp/use92/ Last modified 3/20/1998.

USGS. 1999. The Quality of Our Nation's Waters: Nutrients and Pesticides. U.S. Geological Survey Circular 1225. Reston, VA: United States Geological Survey. 82 pp.

USGS. 2000a. PESTICIDES ANALYZED IN NAWQA SAMPLES: Use, Chemical Analyses, and Water-Quality Criteria (PROVISIONAL DATA -- SUBJECT TO REVISION). Available on the Internet at: http://water.wr.usgs.gov/pnsp/anstrat/ Last modified 8/20/1999.

USGS. 2000b. Pesticides in Surface and Ground Water of the United States: Summary of Results of the National Water Quality Assessment Program (NAWQA). PROVISIONAL DATA -- SUBJECT TO REVISION. Available on the Internet at: http://water.wr.usgs.gov/pnsp/allsum/ Last modified October 9, 1998.

Venkat, J.A., S. Shami, K. Davis, M. Nayak, J.R. Plimmer, R. Pfeil and P.P. Nair. 1995. Relative genotoxic effects of pesticides evaluated by a modified SOS microplate assay. Environmental and Molecular Mutagenesis 25:67-76.

Walker, A. 1978. Simulating of the persistence of eight soil applied herbicides. Weed Res. 19:305-311 (as cited in Burgard, 1994).

Xu, H.H. and K.M. Schurr. 1990. Genotoxicity of 22 pesticides in microtitration SOS chromotest. Tox. Assess. 5: 1-14 (as cited in U.S. EPA 1996).

*Confidential Business Information submitted to the Office of Pesticide Programs.

APPENDIX A: Abbreviations and Acronyms

AA	- Atomic Absorption
ACGIH	- American Conference of Governmental Industrial Hygienists
a.i.	- active ingredient
ANPRM	- Advanced Notice of Proposed Rule-Making
APHA	- American Public Health Association
ARMS	- Agricultural Resources Management Study
ATSDR	- Agency for Toxic Substances and Disease Registry
CA	- Census of Agriculture
CAS	- Chemical Abstract Service
CASRN	- Chemical Abstract Service Registry Number
CCL	- Contaminant Candidate List
CEC	- cation exchange capacity
CERCLA	- Comprehensive Environmental Response, Compensation & Liability Act
CMR	- Chemical Monitoring Reform
CPS	- Cropping Practices Survey
CWS	- Community Water System
DBCP	- dibromochloropropane
DCIs	- Data Call-Ins
DEA	- deethyl-atrazine
DWEL	- Drinking Water Equivalent Level
ECD	- Electron Capture Detectors
EDB	- ethylene dibromide
EDL	- Estimated Detection Limit
Eh	- oxidation-reduction potential
EHS	- Extremely Hazardous Substance
EPA	- Environmental Protection Agency
EPCRA	- Emergency Planning and Community Right-to-Know Act
ESA	- ethanesulfonic acid
FCRS	- Farm Costs and Returns Survey
FDA	- Food and Drug Administration
FIFRA	- Federal Insecticide, Fungicide, and Rodenticide Act
FQPA	- Food Quality Protection Act
GAC	- granular activated carbon (treatment technology for organic compounds)
GC	- gas chromatography (a laboratory method)
GW	- ground water

GWP	- ground water - purchased
GUDI	- Ground Water Under the Direct Influence (of surface water)
GUP	- Ground Water Under Direct Influence - Purchased
HA	- Health Advisory
HAL	- Health Advisory Level
HRL	- Health Reference Level
IDL	- Instrument Detection Level
IGWM	- Iowa Ground Water Monitoring Program
IOC	- inorganic compound
IRIS	- Integrated Risk Information System
MCL	- Maximum Contaminant Level
MDL	- Method Detection Limit
MMT	- methylcyclopentadienyl manganese tricarbonyl
MRL	- Minimum Reporting Level
MS	- mass spectrometry (a laboratory method)
NAWQA	- National Water Quality Assessment Program
NCFAP	- National Center for Food and Agricultural Policy
NCOD	- National Drinking Water Contaminant Occurrence Database
NDWAC	- National Drinking Water Advisory Council
NERL	- National Environmental Research Laboratory
NIOSH	- National Institute for Occupational Safety and Health
NPD	- nitrogen/phosphorus detector
NPDES	- National Pollution Discharge Elimination System
NPDWR	- National Primary Drinking Water Regulation
NPS	- National Pesticide Survey
NRMRL	- National Risk Management Research Laboratory
NTIS	- National Technical Information Service
NTNCWS	- Non-Transient Non-Community Water System
NTTAA	- National Technology Transfer and Advancement Act
OA	- oxanilic acid
OCT	- ornithine-carbamyl transferase
OGWDW	- Office of Ground Water and Drinking Water
OMB	- Office of Management and Budget
ORD	- Office of Research and Development
OSHA	- Occupational Safety and Health Administration
PAH	- polycyclic aromatic hydrocarbon
PB	- particle beam
PBMS	- performance-based measurement system

PCE	- tetrachloroethylene
PEL	- permissible exposure limit
PGWD	- Pesticides in Ground Water Database
ppm	- part per million
PWS	- Public Water System
PWSF	- Public Water System Facility
PWSID	- Public Water System Identifier
QA	- quality assurance
QC	- quality control
RCRA	- Resource Conservation and Recovery Act
RFA	- Regulatory Flexibility Act
RFF	- Resources for the Future
RO	- reverse osmosis
RPD	- relative percent difference
RSD	- relative standard deviation
SARA Title III	- Superfund Amendments and Reauthorization Act
SBREFA	- Small Business Regulatory Enforcement Fairness Act
SD	- standard deviation
SDWA	- Safe Drinking Water Act
SDWIS	- Safe Drinking Water Information System
SDWIS FED	- the Federal Safe Drinking Water Information System
SGOT	- serum glutamate-oxaloacetate transaminase
SGPT	- serum glutamate-pyruvate transaminase
SM	- standard methods
SMCL	- Secondary Maximum Contaminant Level
SMF	- Standard Compliance Monitoring Framework
SOC	- synthetic organic compound
SPE	- solid phase extraction (a laboratory method)
SRF	- State Revolving Fund
STORET	- Storage and Retrieval System
SW	- surface water
SWP	- surface water - purchased
TBD	- to be determined
TCE	- trichloroethylene
TDS	- total dissolved solids
THM	- trihalomethane
TNCWS	- Transient Non-Community Water System
TPQ	- Threshold Planning Quantity
TRI	- Toxic Release Inventory

UCM	- Unregulated Contaminant Monitoring
UCMR	- Unregulated Contaminant Monitoring Regulation/Rule
UMRA	- Unfunded Mandates Reform Act of 1995
URCIS	- Unregulated Contaminant Monitoring Information System
USDA	- United States Department of Agriculture
U.S. EPA	- United States Environmental Protection Agency
USGS	- United States Geological Survey
VOC	- volatile organic compound
µg/L	- micrograms per liter
mg/L	- milligrams per liter
>MCL	- percentage of systems with exceedances
>MRL	- percentage of systems with detections

APPENDIX B: Round 2 Metribuzin Occurrence

Metribuzin Occurrence in Public Water Systems in Round 2, UCM (1993) results

State	Total Unique PWS	# GW PWS	# SW PWS	% PWS > MRL	% GW PWS >MRL	% SW PWS >MRL	% PWS > HRL	% GW PWS > HRL	% SW PWS > HRL	99% Value (µg/L)
Tribes (06)	1	1	0	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
AK	20	17	3	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
AL										
AR	536	431	105	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
AZ										
CA										
CO	750	538	212	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
CT	69	35	34	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
IN										
KY	418	204	214	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 10.00
LA										
MA	56	29	27	14.29%	13.79%	14.81%	0.00%	0.00%	0.00%	2.00
MD	684	627	57	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.30
ME										
MI	2,650	2,570	80	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
MN	1,264	1,234	30	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
MO	638	437	101	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.60
MS										
NC	623	567	56	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
ND	296	258	38	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.02
NH	557	524	33	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
NJ										
NM	715	686	29	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.60
OH	2,178	2,017	161	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 2.00
OK	107	82	25	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
OR	1,135	984	151	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
PA	358	231	127	9.50%	5.63%	16.54%	0.00%	0.00%	0.00%	3.00
RI	15	6	9	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.53

Appendix B (continued)

State	Total Unique PWS	# GW PWS	# SW PWS	% PWS > MRL	% GW PWS >MRL	% SW PWS >MRL	% PWS > HRL	% GW PWS > HRL	% SW PWS > HRL	99% Value (µg/L)
SC	940	842	98	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
SD										
TN	7	2	5	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
TX	426	121	305	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.20
VT	390	338	52	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	< 0.00
WA	600	530	70	0.17%	0.19%	0.00%	0.00%	0.00%	0.00%	< 0.00
WI										
Total	15,333	13,311	2,022	0.28%	0.14%	1.24%	0.00%	0.00%	0.00%	< 2.00
20 States	13,568	11,862	1,706	0.07%	0.04%	0.23%	0.00%	0.00%	0.00%	< 2.00
19 States	13,512	11,833	1,697	0.01%	0.01%	0.00%	0.00%	0.00%	0.00%	< 2.00

1. Massachusetts data not included in "19 States" summary for metribuzin.
PWS = Public Water System; GW = Ground Water (PWS Source Water Type); SW = Surface Water (PWS Source Water Type); MRL = Minimum Reporting Limit (for laboratory analyses)
The Health Reference Level (HRL) is the estimated health effect level as provided by EPA for preliminary assessment for this work assignment.
"% > HRL" indicates the proportion of systems with any analytical results exceeding the concentration value of the HRL.
The Health Reference Level (HRL) used for Metribuzin is 91 µg/L. This is a draft value for working review only.
The highlighted States are part of the SDWI/FED 20 State Cross-Section.