

Organophosphate Pesticides: Specific Metabolites

General Information

These metabolites differ from the dialkyl phosphates because each specific metabolite derives from one or only a few parent pesticides. Table 272 shows the parent organophosphate pesticides and their metabolites. For example, malathion is metabolized to malathion dicarboxylic acid. *Para*-nitrophenol is a metabolite of parathion and methyl parathion and other chemicals. Chlorpyrifos and chlorpyrifos methyl are metabolized to 3,5,6-trichloro-2-pyridinol. In addition to reflecting exposure to the parent insecticide, the level of these metabolites in a person's urine may also reflect exposure to the metabolite if it was present in the person's food or environment.

Sources of potential exposure to organophosphates vary, depending on the chemical. Some organophosphates (including malathion and chlorpyrifos) are commonly used in agriculture, whereas the use of other organophosphates (such as parathion and methyl parathion) have been restricted significantly in the United States. Some organophosphates (malathion, naled) are used for the public health control of mosquitoes. The U.S. FDA, USDA, U.S. EPA, and OSHA have developed criteria on allowable levels of these chemicals in foods, the environment, and the workplace, respectively.

The organophosphates share a common mechanism of toxicity that occurs through inhibition of the enzyme acetylcholinesterase in the nervous system. Symptoms of an acute overexposure may include nausea, vomiting, cholinergic effects, weakness, paralysis, and seizures. The specific metabolites reported in this section do not inhibit acetylcholinesterase enzymes but rather are an indicator of exposure to the parent compounds.

This *Report* provides measurements for the metabolites of six organophosphate pesticides. Information about external exposure (i.e., environmental levels) and health effects of specific organophosphate pesticides is available from the U.S. EPA's IRIS Web site at <http://www.epa.gov/iris> and from ATSDR's Toxicological Profiles at <http://www.atsdr.cdc.gov/toxprofiles>.

Table 271. Organophosphate pesticides: specific metabolites

Organophosphate pesticide (CAS number)	Primary urinary metabolite (CAS number)
Malathion (121-75-5)	Malathion dicarboxylic acid (1190-28-9)
Parathion (56-38-2)	<i>para</i> -Nitrophenol (100-02-7)
Methyl parathion (298-00-0)	<i>para</i> -Nitrophenol (100-02-7)
Chlorpyrifos (2921-88-2)	3,5,6-Trichloro-2-pyridinol (6515-38-4)
Chlorpyrifos methyl (5598-13-0)	3,5,6-Trichloro-2-pyridinol (6515-38-4)
Diazinon (333-41-5)	2-Isopropyl-4-methyl-6-hydroxypyrimidine (2814-20-2)
Pirimiphos methyl (29232-93-7)	2-(Diethylamino)-6-methylpyrimidin-4-ol/one
Coumaphos (56-72-4)	3-Chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol

Malathion Dicarboxylic Acid

CAS No. 1190-28-9

Metabolite of Malathion, CAS No. 121-75-5

General Information

Malathion dicarboxylic acid is a metabolite of malathion, which is an organophosphate insecticide that is used on a variety of agricultural crops. There are also non-agricultural uses of this insecticide on lawns, gardens, ornamental trees, shrubs, and plants. Malathion is registered for use in public health mosquito control and in government programs such as the USDA's Boll Weevil Eradication Program. Approximately 16.7 million pounds of malathion, most of which is applied to cotton, are used annually in the United States. Malathion is also used medically in lotion form (0.5%) to kill body lice.

In addition to being a metabolite of malathion in the body, malathion dicarboxylic acid can also occur in the environment from the breakdown of the parent compound. Thus, the detection of malathion dicarboxylic acid in a person's urine may also reflect exposure to the metabolite if it was present in a person's food or environment.

Malathion is slowly absorbed through the skin but is more rapidly and efficiently absorbed via ingestion. It is

metabolized in the body to malaoxon, malathion monocarboxylic acid, malathion dicarboxylic acid, and dialkylphosphate metabolites (see section titled "Organophosphate Pesticides: Dialkyl Phosphate Metabolites"). Malathion is rapidly eliminated from the body within 12-24 hours (Bouchard et al., 2003).

Symptoms of an acute overdose of malathion may include nausea, vomiting, cholinergic effects, weakness, paralysis, and seizures. Compared with other organophosphate insecticides, malathion has low acute toxicity. Malathion does not appear to produce human reproductive or teratogenic effects at environmental levels of exposure in human populations (Thomas et al., 1990; Grether et al., 1987). IARC considers malathion not classifiable as a human carcinogen.

Interpreting Levels of Urinary Malathion Dicarboxylic Acid Reported in the Tables

Levels of urinary malathion dicarboxylic acid were measured in a subsample of NHANES participants aged 6-59 years. Note that no data are available for the NHANES 2001-2002 subsample. Participants were selected within the specified age range to be a

Table 272. Malathion dicarboxylic acid

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	< LOD	< LOD	1920
Age group							
6-11 years	99-00	*	< LOD	< LOD	< LOD	2.80 (<LOD-5.50)	453
12-19 years	99-00	*	< LOD	< LOD	< LOD	< LOD	660
20-59 years	99-00	*	< LOD	< LOD	< LOD	< LOD	807
Gender							
Males	99-00	*	< LOD	< LOD	< LOD	< LOD	937
Females	99-00	*	< LOD	< LOD	< LOD	< LOD	983
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	< LOD	< LOD	< LOD	680
Non-Hispanic blacks	99-00	*	< LOD	< LOD	< LOD	< LOD	498
Non-Hispanic whites	99-00	*	< LOD	< LOD	< LOD	< LOD	580

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

representative sample of the U.S. population. For the NHANES 1999-2000 subsample, urinary levels of malathion dicarboxylic acid at the 95th percentile in children aged 6-11 years are several-fold lower than levels that were measured in Minnesota children (aged 3-13 years, adjusted for sociodemographic variables) in 1997 (Adgate, 2001). In this Minnesota study, children from an urban setting had urinary levels of malathion dicarboxylic acid that were similar to levels in children from a nonurban setting. Of 382 pregnant women living in an agricultural community, 30% had detectable levels of malathion dicarboxylic acid at a detection limit about ten-fold lower than the detection limit used in the NHANES 1999-2000 analyses (Eskenazi et al., 2004). A study of agricultural workers reported urinary levels of malathion dicarboxylic acid ranging from 4-10 µg/gram creatinine, and no effect on cholinesterase activity was observed in these workers (Krieger and Dinoff, 2000). Such worker values are only slightly higher than those detected in the NHANES 1999-2000 subsample.

Finding a measurable amount of malathion dicarboxylic acid in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to malathion and health effects. These data also provide physicians with a reference range so that they can determine whether or not other people have been exposed to higher levels of malathion than those levels found in the general population.

Table 273. Malathion dicarboxylic acid (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2000.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	< LOD	< LOD	1920
Age group							
6-11 years	99-00	*	< LOD	< LOD	< LOD	3.74 (2.11-5.50)	453
12-19 years	99-00	*	< LOD	< LOD	< LOD	< LOD	660
20-59 years	99-00	*	< LOD	< LOD	< LOD	< LOD	807
Gender							
Males	99-00	*	< LOD	< LOD	< LOD	< LOD	937
Females	99-00	*	< LOD	< LOD	< LOD	< LOD	983
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	< LOD	< LOD	< LOD	680
Non-Hispanic blacks	99-00	*	< LOD	< LOD	< LOD	< LOD	498
Non-Hispanic whites	99-00	*	< LOD	< LOD	< LOD	< LOD	580

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

para-Nitrophenol

CAS No. 100-02-7

*Metabolite of Methyl Parathion, CAS No.298-00-0 and Ethyl Parathion, CAS No. 56-38-2***General Information**

Para-nitrophenol is a metabolite of the pesticides methyl parathion, ethyl parathion, O-ethyl 4-nitrophenyl phenylphosphonothioate, and of nitrobenzene, which is not a pesticide. Methyl parathion is a restricted-use pesticide with limited applications in agriculture, and many agricultural uses of methyl parathion have been cancelled. Past peak domestic use was once as high as 4 million pounds per year. Methyl parathion is not registered for residential use in the United States. Ethyl parathion had been a restricted-use pesticide with limited applications on certain agricultural crops, but in 2002 voluntary cancellation of all registrations occurred.

In addition to being a metabolite of methyl and ethyl parathion in the body, *para*-nitrophenol can also occur in the environment from the breakdown of the parent compounds. Thus, the detection of *para*-nitrophenol in a person's urine may also reflect exposure to the metabolite if it was present in a person's food or environment

In animal studies, methyl parathion is rapidly absorbed after ingestion, more slowly absorbed through the skin, and is eliminated rapidly after exposure (Kramer et al., 2002). In addition to being metabolized to *para*-nitrophenol, parathion and methyl parathion are metabolized to dialkyl phosphates (see section titled "Organophosphate Pesticides: Dialkyl Phosphate Metabolites").

Table 274. para-Nitrophenol

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	2.40 (1.40-4.50)	5.00 (2.90-11.0)	1989
	01-02	*	< LOD	1.32 (1.20-1.48)	2.70 (2.40-3.02)	3.70 (3.38-3.93)	2477
Age group							
6-11 years	99-00	*	< LOD	.910 (<LOD-2.40)	2.63 (1.70-3.80)	4.20 (2.70-6.40)	479
	01-02	*	.790 (<LOD-.910)	1.48 (1.34-1.61)	2.83 (2.22-3.58)	3.90 (3.01-4.74)	565
12-19 years	99-00	*	< LOD	< LOD	3.40 (1.60-5.70)	5.70 (2.60-19.0)	680
	01-02	*	.720 (<LOD-.910)	1.44 (1.32-1.61)	2.61 (2.15-3.11)	3.34 (3.11-4.01)	813
20-59 years	99-00	*	< LOD	< LOD	2.30 (1.20-5.30)	4.50 (2.20-9.50)	830
	01-02	*	< LOD	1.27 (1.08-1.45)	2.69 (2.32-3.10)	3.72 (3.37-4.24)	1099
Gender							
Males	99-00	*	< LOD	< LOD	2.40 (1.40-4.20)	4.40 (2.50-12.0)	971
	01-02	*	.760 (.300-.910)	1.49 (1.30-1.66)	2.99 (2.59-3.23)	4.00 (3.37-4.91)	1164
Females	99-00	*	< LOD	< LOD	2.50 (1.30-5.70)	5.20 (2.90-9.50)	1018
	01-02	*	< LOD	1.18 (.990-1.37)	2.26 (1.92-2.69)	3.46 (3.18-3.71)	1313
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	1.60 (<LOD-3.40)	5.80 (2.60-23.0)	21.0 (3.50-36.0)	695
	01-02	*	.690 (<LOD-.840)	1.32 (1.08-1.54)	2.62 (1.91-3.44)	3.85 (2.70-6.05)	660
Non-Hispanic blacks	99-00	*	< LOD	1.17 (<LOD-2.50)	2.90 (1.70-6.00)	4.80 (2.50-9.20)	518
	01-02	*	.860 (<LOD-1.12)	1.80 (1.37-2.16)	3.21 (2.55-4.38)	5.60 (4.02-6.79)	679
Non-Hispanic whites	99-00	*	< LOD	< LOD	2.10 (<LOD-4.70)	4.20 (2.10-11.0)	603
	01-02	*	< LOD	1.27 (1.11-1.42)	2.71 (2.30-3.10)	3.70 (3.28-4.01)	941

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Symptoms of an acute overdose of methyl or ethyl parathion may include nausea, vomiting, cholinergic effects, weakness, paralysis, and seizures. Delayed peripheral neuropathy has been reported after chronic occupational exposure and acute overdose. The metabolite, *para*-nitrophenol, does not inhibit acetylcholinesterase enzymes. IARC does not consider ethyl parathion and methyl parathion classifiable as human carcinogens.

Interpreting Levels of Urinary *para*-Nitrophenol Reported in the Tables

Urinary levels of *para*-nitrophenol were measured in a subsample of NHANES participants aged 6-59 years. Participants were selected within the specified age range to be a representative sample of the U.S. population. In general, urinary *para*-nitrophenol levels in the NHANES 2001-2002 subsample appeared roughly similar to values in a nonrandom subsample of NHANES III (1988-1994) participants (Hill et al., 1995).

Considerably higher levels of *para*-nitrophenol have been measured in urine samples obtained from children and adults living in residences where methyl parathion was illegally applied indoors (Barr et al., 2002). The geometric mean concentration of *para*-nitrophenol in these individuals was approximately nine times higher than the 95th percentile values for the 2001-2002 NHANES subsample. In a study of workers who handle parathion, end-of-shift urinary *para*-nitrophenol levels ranged from 190-410 µg/gram of creatinine (Leng and Lewalter, 1999), a range of values that is much higher than the 95th percentile values in this *Report*. ACGIH (2001) recommends a BEI of 0.5 mg (500 µg)/g creatinine for workers at the end of shift.

Finding a measurable amount of *para*-nitrophenol in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to methyl or ethyl parathion and health effects.

Table 275. *para*-Nitrophenol (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	2.08 (1.33-3.91)	4.20 (2.15-10.2)	1989
	01-02	*	< LOD	.968 (.826-1.10)	1.91 (1.72-2.03)	2.89 (2.44-3.23)	2476
Age group							
6-11 years	99-00	*	< LOD	.938 (.609-1.95)	2.80 (1.94-4.00)	4.20 (3.33-6.70)	479
	01-02	*	.715 (.543-.870)	1.59 (1.30-1.82)	2.74 (2.31-3.11)	3.67 (3.11-4.61)	565
12-19 years	99-00	*	< LOD	< LOD	1.79 (1.08-3.04)	4.00 (1.57-7.29)	680
	01-02	*	.372 (.250-.503)	.839 (.790-.951)	1.59 (1.37-1.78)	2.09 (1.78-2.43)	812
20-59 years	99-00	*	< LOD	< LOD	2.00 (1.17-4.08)	4.29 (2.13-12.3)	830
	01-02	*	< LOD	.875 (.693-1.07)	1.79 (1.56-2.05)	2.89 (2.35-3.33)	1099
Gender							
Males	99-00	*	< LOD	< LOD	1.90 (1.01-3.39)	3.39 (1.77-7.55)	971
	01-02	*	.430 (.307-.535)	.983 (.854-1.08)	1.87 (1.57-2.09)	2.97 (2.14-3.57)	1164
Females	99-00	*	< LOD	< LOD	2.22 (1.48-4.88)	6.90 (2.76-14.1)	1018
	01-02	*	< LOD	.933 (.735-1.23)	1.96 (1.78-2.15)	2.81 (2.44-3.06)	1312
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	1.53 (.759-3.17)	4.80 (2.21-21.9)	17.4 (3.94-47.7)	695
	01-02	*	.402 (.219-.543)	.928 (.717-1.20)	1.87 (1.41-2.60)	3.04 (2.38-3.84)	660
Non-Hispanic blacks	99-00	*	< LOD	.667 (.314-1.79)	2.07 (1.33-3.71)	3.71 (1.98-7.20)	518
	01-02	*	.436 (.167-.636)	1.01 (.801-1.31)	1.71 (1.60-2.21)	2.97 (2.16-4.30)	678
Non-Hispanic whites	99-00	*	< LOD	< LOD	1.94 (1.07-4.29)	3.75 (1.97-10.2)	603
	01-02	*	< LOD	.967 (.786-1.13)	1.96 (1.67-2.26)	2.93 (2.35-3.45)	941

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

These data also provide physicians with a reference range so that they can determine whether or not other people have been exposed to higher levels of methyl and ethyl parathion than those levels found in the general population.

3,5,6-Trichloro-2-pyridinol

CAS No. 6515-38-4

Metabolite of Chlorpyrifos, CAS No. 2921-88-2 and Chlorpyrifos-methyl, CAS No. 5598-13-0

General Information

The chemical 3,5,6-trichloro-2-pyridinol (TCPy) is a specific metabolite of chlorpyrifos and chlorpyrifos-methyl. Chlorpyrifos is an organophosphate insecticide that is used to control insect pests on a variety of agricultural crops in the United States. Approximately 10 million pounds have been applied annually in agriculture. Chlorpyrifos is no longer registered for most indoor residential uses in the United States. Not registered for residential use, chlorpyrifos-methyl is an organophosphate pesticide used in agriculture. Approximately 80,000 pounds are used per year.

In addition to being a metabolite of chlorpyrifos and chlorpyrifos-methyl in the body, TCPy can also occur in the environment from the breakdown of the parent

compounds. Thus, the detection of TCPy in a person's urine may also reflect exposure to the metabolite if it was present in a person's food or environment. In 142 urban homes and preschools of North Carolina, chlorpyrifos and TCPy were detected in all indoor air and dust samples (Morgan et al., 2004)

Chlorpyrifos is not well absorbed through the skin but is rapidly absorbed once ingested. Nolan et al. (1984) found that TCPy is eliminated from the body in the urine with a half-life of approximately 27 hours. Chlorpyrifos, chlorpyrifos-methyl, and other organophosphate pesticides share a common mechanism of toxicity, inhibiting the activity of acetylcholinesterase enzymes in the nervous system. The metabolite TCPy does not inhibit acetylcholinesterase enzymes.

Table 276. 3,5,6-Trichloro-2-pyridinol

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

	Survey years	Geometric mean	Selected percentiles				Sample size
		(95% conf. interval)	(95% confidence interval)				
			50th	75th	90th	95th	
Total, age 6 and older	99-00	1.77 (1.46-2.14)	1.70 (1.40-2.10)	3.50 (2.50-5.10)	7.30 (4.80-10.0)	9.90 (7.60-14.0)	1994
	01-02	1.76 (1.52-2.03)	2.20 (1.86-2.61)	4.95 (4.55-5.29)	8.80 (7.74-9.77)	12.4 (10.4-15.3)	2509
Age group							
6-11 years	99-00	2.88 (1.99-4.16)	2.70 (1.60-4.80)	6.90 (3.40-10.0)	11.0 (7.70-17.0)	16.0 (10.0-26.0)	481
	01-02	2.67 (2.13-3.35)	3.08 (2.46-4.22)	6.36 (4.97-7.97)	10.7 (7.98-15.3)	14.9 (11.5-24.0)	573
12-19 years	99-00	2.37 (1.89-2.97)	2.10 (1.60-2.90)	4.50 (2.90-6.70)	8.00 (5.50-14.0)	12.5 (8.00-24.0)	681
	01-02	2.71 (2.19-3.35)	3.57 (2.60-4.30)	6.57 (5.61-7.59)	11.2 (8.66-15.1)	18.0 (13.7-23.7)	823
20-59 years	99-00	1.53 (1.29-1.82)	1.50 (1.20-1.70)	2.80 (2.20-4.10)	5.90 (3.90-8.90)	8.60 (6.70-11.0)	832
	01-02	1.51 (1.32-1.72)	1.91 (1.44-2.26)	4.42 (3.90-4.80)	7.78 (7.00-8.91)	10.9 (9.52-12.4)	1113
Gender							
Males	99-00	1.92 (1.60-2.32)	1.90 (1.50-2.40)	3.50 (2.70-5.60)	7.30 (5.04-10.0)	9.90 (7.40-14.0)	972
	01-02	2.13 (1.81-2.51)	2.66 (2.19-3.16)	5.37 (4.83-6.25)	9.63 (8.20-11.3)	14.9 (10.9-18.9)	1183
Females	99-00	1.63 (1.31-2.02)	1.50 (1.20-1.80)	3.30 (2.30-5.30)	7.20 (4.30-12.0)	10.0 (7.10-15.0)	1022
	01-02	1.45 (1.24-1.70)	1.72 (1.39-2.21)	4.38 (3.72-4.95)	7.71 (6.30-9.20)	10.4 (8.47-13.2)	1326
Race/ethnicity							
Mexican Americans	99-00	1.61 (1.31-2.00)	1.67 (1.30-2.20)	3.20 (2.60-3.80)	5.00 (3.80-7.30)	7.40 (5.10-17.0)	697
	01-02	2.02 (1.79-2.28)	2.63 (2.24-3.01)	4.55 (4.05-5.39)	9.02 (7.04-10.8)	12.2 (10.8-15.7)	660
Non-Hispanic blacks	99-00	2.17 (1.59-2.97)	1.90 (1.40-2.70)	4.20 (2.50-8.30)	9.40 (6.30-12.9)	13.0 (9.40-26.0)	521
	01-02	2.19 (1.68-2.84)	2.89 (2.28-3.47)	5.47 (4.77-6.96)	9.27 (7.47-11.6)	12.3 (10.1-16.8)	701
Non-Hispanic whites	99-00	1.76 (1.51-2.05)	1.60 (1.50-2.00)	3.40 (2.50-4.80)	7.10 (4.30-10.5)	10.0 (7.20-14.0)	602
	01-02	1.71 (1.43-2.03)	2.15 (1.62-2.64)	4.94 (4.41-5.31)	8.68 (7.47-9.97)	12.3 (9.77-15.9)	947

Interpreting Levels of Urinary TCPy Reported in the Tables

Urinary TCPy levels were measured in a subsample of NHANES participants aged 6-59 years. Participants were selected within the specified age range to be a representative sample of the U.S. population. In the current NHANES 2001-2002 subsample, TCPy levels appeared roughly similar to values reported for a nonrandom subsample of NHANES III (1988-1994) participants (Hill et al., 1995) and to levels reported in a studies of healthy adults in Germany (Koch et al., 2001) and Italy (Aprea et al., 1999). In a probability-based sample of 102 Minnesota children aged 3-13 years, the weighted population mean of TCPy measurements was approximately three times higher (Adgate, 2001) than the corresponding values reported for the group aged 6-11 years in this *Report*. In another study of adults in Maryland, MacIntosh et al. (1999) found that mean urinary TCPy levels were about three times higher than the levels for adults documented in this *Report*. Of 482 pregnant women living in an agricultural community,

76% had detectable levels of TCPy, and levels were similar to those reported for NHANES 1999-2000 (Eskenazi et al., 2004). Higher levels of TCPy have been measured in urine samples obtained from pesticide applicators. In one study of male pesticide applicators, the geometric mean levels of TCPy in urine samples ranged from 169-262 µg/g creatinine (Hines et al., 2001). These levels are more than 100-fold higher than the geometric mean values for males documented in this *Report*.

Comparing Adjusted Geometric Means

Geometric mean levels of urinary TCPy for the demographic groups were compared after adjusting for the covariates of race/ethnicity, age, gender, and urinary creatinine (data not shown). In NHANES 2002-2002, the group aged 6-11 years had higher adjusted geometric mean levels of urinary TCPy than the other two age groups, and the group aged 12-19 years had slightly higher urinary levels of TCPy than the group aged 20-59 years. It is unknown whether these differences associated

Table 277. 3,5,6-Trichloro-2-pyridinol (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

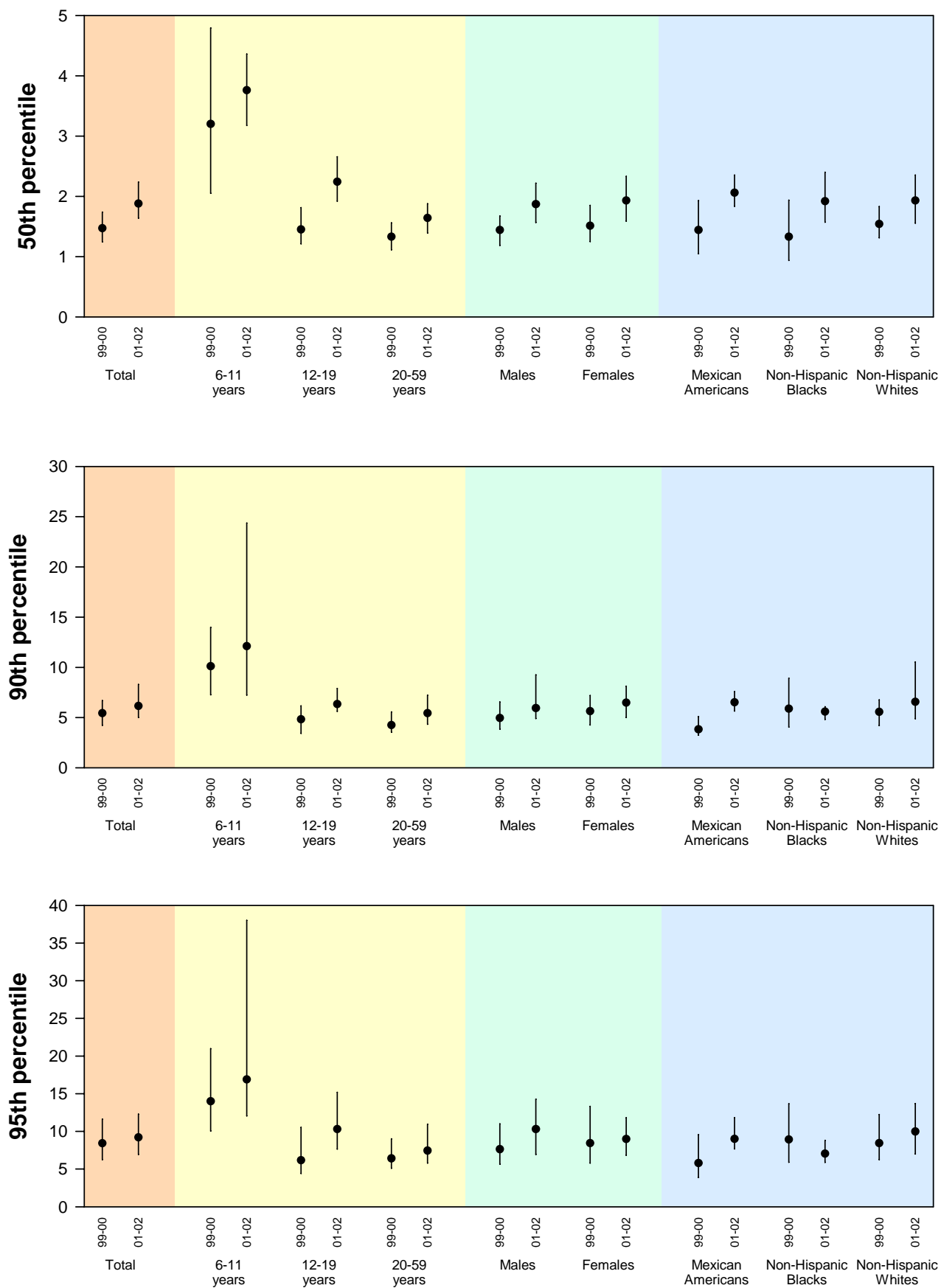
	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	1.58 (1.35-1.85)	1.47 (1.24-1.74)	2.85 (2.11-3.59)	5.43 (4.22-6.68)	8.42 (6.25-11.6)	1994
	01-02	1.73 (1.49-2.01)	1.88 (1.64-2.24)	3.76 (2.91-4.62)	6.15 (4.99-8.31)	9.22 (6.94-12.3)	2508
Age group							
6-11 years	99-00	3.11 (2.31-4.19)	3.20 (2.05-4.80)	6.37 (4.14-8.19)	10.1 (7.26-14.0)	14.0 (10.1-21.0)	481
	01-02	3.48 (2.80-4.32)	3.76 (3.17-4.36)	6.21 (4.88-8.57)	12.1 (7.24-24.4)	16.9 (12.1-38.0)	573
12-19 years	99-00	1.60 (1.34-1.91)	1.45 (1.21-1.81)	2.58 (1.97-3.92)	4.82 (3.44-6.16)	6.16 (4.43-10.6)	681
	01-02	2.09 (1.72-2.55)	2.24 (1.92-2.66)	3.97 (3.30-4.72)	6.33 (5.62-7.89)	10.3 (7.65-15.2)	822
20-59 years	99-00	1.41 (1.23-1.62)	1.33 (1.11-1.56)	2.37 (1.87-3.01)	4.25 (3.53-5.56)	6.42 (5.11-9.02)	832
	01-02	1.49 (1.30-1.71)	1.64 (1.39-1.88)	3.11 (2.60-3.91)	5.43 (4.33-7.23)	7.44 (5.80-11.0)	1113
Gender							
Males	99-00	1.48 (1.27-1.72)	1.44 (1.19-1.68)	2.52 (2.05-3.38)	4.95 (3.84-6.54)	7.63 (5.65-11.0)	972
	01-02	1.71 (1.47-2.00)	1.87 (1.57-2.22)	3.46 (2.82-4.28)	5.93 (4.90-9.24)	10.3 (6.94-14.3)	1183
Females	99-00	1.69 (1.42-2.01)	1.51 (1.25-1.85)	2.96 (2.24-4.01)	5.63 (4.26-7.19)	8.44 (5.79-13.3)	1022
	01-02	1.75 (1.49-2.07)	1.93 (1.59-2.33)	3.91 (3.06-4.85)	6.47 (5.00-8.11)	8.98 (6.83-11.8)	1325
Race/ethnicity							
Mexican Americans	99-00	1.46 (1.20-1.77)	1.44 (1.05-1.93)	2.38 (2.09-2.96)	3.82 (3.24-5.08)	5.79 (3.88-9.57)	697
	01-02	1.86 (1.63-2.12)	2.06 (1.83-2.35)	3.81 (3.17-4.56)	6.52 (5.64-7.58)	9.00 (7.66-11.8)	660
Non-Hispanic blacks	99-00	1.47 (1.09-1.99)	1.33 (.936-1.94)	2.86 (1.58-5.05)	5.88 (4.05-8.93)	8.93 (5.91-13.7)	521
	01-02	1.56 (1.19-2.03)	1.92 (1.57-2.40)	3.52 (2.85-4.28)	5.58 (4.80-6.08)	7.06 (5.88-8.82)	700
Non-Hispanic whites	99-00	1.66 (1.45-1.90)	1.54 (1.31-1.83)	2.93 (2.09-3.97)	5.56 (4.21-6.75)	8.44 (6.25-12.3)	602
	01-02	1.78 (1.49-2.14)	1.93 (1.56-2.35)	3.82 (2.70-4.97)	6.55 (4.88-10.5)	9.98 (7.00-13.7)	947

with age represent differences in exposure, pharmacokinetics, or the relationship of dose per body weight.

Finding a measurable amount of TCPy in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to chlorpyrifos or chlorpyrifos-methyl and health effects. These data also provide physicians with a reference range so that they can determine whether or not other people have been exposed to higher levels of chlorpyrifos or chlorpyrifos-methyl than those levels found in the general population.

Figure 36. 3,5,6-Trichloro-2-pyridinol (creatinine corrected)

Selected percentiles with 95% confidence intervals of urine concentrations (in $\mu\text{g/g}$ of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.



^a Estimate is less than the limit of detection (LOD). See Appendix A for LODs.

2-Isopropyl-4-methyl-6-hydroxypyrimidine

CAS No. 2814-20-2

Metabolite of Diazinon, CAS No. 333-41-5

General Information

The specific metabolite of diazinon is 2-isopropyl-4-methyl-6-hydroxypyrimidine. Diazinon is an organophosphate insecticide that is used to control pests on certain agricultural commodities (including almonds and fruits that contain stones or pits). It is also used as a veterinary insecticide on cattle. Approximately 13 million pounds of diazinon are used annually on agricultural sites in the United States, but diazinon is no longer registered for indoor residential use.

In addition to being a metabolite of diazinon in the body, 2-isopropyl-4-methyl-6-hydroxypyrimidine can also occur in the environment from the breakdown of the

parent compound. Thus, the detection of 2-isopropyl-4-methyl-6 hydroxypyrimidine in a person's urine may also reflect exposure to the metabolite if it was present in a person's food or environment.

Diazinon is not well-absorbed through the skin but is rapidly absorbed in the body once ingested. Experimental diazinon exposure in people has shown a rapid elimination from the body, as inferred from dialkyl phosphate excretion (Garfitt et al., 2002). Diazinon and other organophosphates share a common mechanism of toxicity, inhibiting the activity of acetylcholinesterase enzymes in the nervous system. The metabolite 2-isopropyl-4-methyl-6-hydroxypyrimidine does not inhibit acetylcholinesterase enzymes.

Table 278. 2-Isopropyl-4-methyl-6-hydroxypyrimidine

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	< LOD	< LOD	1842
	01-02	*	< LOD	< LOD	< LOD	< LOD	2535
Age group							
6-11 years	99-00	*	< LOD	< LOD	< LOD	< LOD	454
	01-02	*	< LOD	< LOD	< LOD	1.45 (<LOD-3.11)	580
12-19 years	99-00	*	< LOD	< LOD	< LOD	< LOD	632
	01-02	*	< LOD	< LOD	< LOD	< LOD	829
20-59 years	99-00	*	< LOD	< LOD	< LOD	< LOD	756
	01-02	*	< LOD	< LOD	< LOD	< LOD	1126
Gender							
Males	99-00	*	< LOD	< LOD	< LOD	< LOD	894
	01-02	*	< LOD	< LOD	< LOD	< LOD	1191
Females	99-00	*	< LOD	< LOD	< LOD	< LOD	948
	01-02	*	< LOD	< LOD	< LOD	< LOD	1344
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	< LOD	< LOD	< LOD	644
	01-02	*	< LOD	< LOD	< LOD	< LOD	678
Non-Hispanic blacks	99-00	*	< LOD	< LOD	< LOD	< LOD	484
	01-02	*	< LOD	< LOD	< LOD	1.35 (<LOD-1.98)	700
Non-Hispanic whites	99-00	*	< LOD	< LOD	< LOD	< LOD	554
	01-02	*	< LOD	< LOD	< LOD	< LOD	956

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Interpreting Levels of Urinary 2-Isopropyl-4-methyl-6-hydroxypyrimidine Reported in the Tables

Urinary levels of 2-isopropyl-4-methyl-6-hydroxypyrimidine were measured in a subsample of NHANES participants aged 6-59 years. Participants were selected within the specified age range to be a representative sample of the U.S. population. In the NHANES 2001-2002 subsample, most of the measurements of 2-isopropyl-4-methyl-6-hydroxypyrimidine in urine were below the limit of detection. In a previous nonrandom sample of adults and children in the United States, 2-isopropyl-4-methyl-6-

hydroxypyrimidine levels in urine ranged from non-detectable to 10 µg/L (Baker et al., 2000).

Finding a measurable amount of 2-isopropyl-4-methyl-6-hydroxypyrimidine in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to diazinon and health effects. These data also provide physicians with a reference range so that they can determine whether or not other people have been exposed to higher levels of diazinon than those levels found in the general population.

Table 279. 2-Isopropyl-4-methyl-6-hydroxypyrimidine (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	99-00	*	< LOD	< LOD	< LOD	< LOD	1842
	01-02	*	< LOD	< LOD	< LOD	< LOD	2534
Age group							
6-11 years	99-00	*	< LOD	< LOD	< LOD	< LOD	454
	01-02	*	< LOD	< LOD	< LOD	2.58 (1.75-4.45)	580
12-19 years	99-00	*	< LOD	< LOD	< LOD	< LOD	632
	01-02	*	< LOD	< LOD	< LOD	< LOD	828
20-59 years	99-00	*	< LOD	< LOD	< LOD	< LOD	756
	01-02	*	< LOD	< LOD	< LOD	< LOD	1126
Gender							
Males	99-00	*	< LOD	< LOD	< LOD	< LOD	894
	01-02	*	< LOD	< LOD	< LOD	< LOD	1191
Females	99-00	*	< LOD	< LOD	< LOD	< LOD	948
	01-02	*	< LOD	< LOD	< LOD	< LOD	1343
Race/ethnicity							
Mexican Americans	99-00	*	< LOD	< LOD	< LOD	< LOD	644
	01-02	*	< LOD	< LOD	< LOD	< LOD	678
Non-Hispanic blacks	99-00	*	< LOD	< LOD	< LOD	< LOD	484
	01-02	*	< LOD	< LOD	< LOD	1.76 (1.07-3.48)	699
Non-Hispanic whites	99-00	*	< LOD	< LOD	< LOD	< LOD	554
	01-02	*	< LOD	< LOD	< LOD	< LOD	956

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

2-(Diethylamino)-6-methylpyrimidin-4-ol/one

Metabolite of Pirimiphos-methyl, CAS No. 29232-93-7

General Information

The chemical 2-(diethylamino)-6-methylpyrimidin-4-ol/one is a specific metabolite of the organophosphate insecticide pirimiphos-methyl. Pirimiphos-methyl has limited applications in agriculture but is used as a veterinary insecticide. It is not registered for residential use in the United States.

In addition to being a metabolite of pirimiphos-methyl in the body, 2-(diethylamino)-6-methylpyrimidin-4-ol/one can also occur in the environment. Thus, the detection of 2-(diethylamino)-6-methylpyrimidin-4-ol/one may also reflect exposure to the metabolite if it was present in a person's food or environment. Pirimiphos-methyl and other organophosphate pesticides share a common mechanism of toxicity, inhibiting the activity of acetylcholinesterase enzymes in the nervous system. Pirimiphos-methyl has generally been shown to be of low acute toxicity. The metabolite 2-(diethylamino)-6-methylpyrimidin-4-ol/one does not inhibit acetylcholinesterase enzymes.

Interpreting Levels of Urinary 2-(Diethylamino)-6-methylpyrimidin-4-ol/one Reported in the Tables

Urinary levels of 2-(diethylamino)-6-methylpyrimidin-4-ol/one were measured in a subsample of NHANES participants aged 6 years and older. Participants were selected within the specified age range to be a representative sample of the U.S. population. In the NHANES 2001-2002 subsample, most urinary levels of 2-(diethylamino)-6-methylpyrimidin-4-ol/one were below the limit of detection. In a study of urine specimens obtained from a nonrandom sample of adults and children in the United States, Olsson et al. (2003) found that the geometric mean concentration of 2-(diethylamino)-6-methylpyrimidin-4-ol/one was 4.1 ng/mL urine, with values ranging from non-detectable to 37 ng/mL.

Finding a measurable amount of 2-(diethylamino)-6-methylpyrimidin-4-ol/one in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to pirimiphos-methyl and health effects. These data also provide physicians with a

Table 280. 2-(Diethylamino)-6-methylpyrimidin-4-ol/one

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 2001-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	01-02	*	< LOD	< LOD	< LOD	.470 (.210-.730)	2481
Age group							
6-11 years	01-02	*	< LOD	< LOD	.230 (<LOD-.820)	.820 (.210-1.64)	567
12-19 years	01-02	*	< LOD	< LOD	< LOD	.610 (<LOD-1.94)	810
20-59 years	01-02	*	< LOD	< LOD	< LOD	.430 (<LOD-.670)	1104
Gender							
Males	01-02	*	< LOD	< LOD	< LOD	.840 (.300-1.55)	1165
Females	01-02	*	< LOD	< LOD	< LOD	.200 (<LOD-.460)	1316
Race/ethnicity							
Mexican Americans	01-02	*	< LOD	< LOD	< LOD	.400 (<LOD-1.15)	669
Non-Hispanic blacks	01-02	*	< LOD	< LOD	< LOD	< LOD	687
Non-Hispanic whites	01-02	*	< LOD	< LOD	< LOD	.490 (.200-.840)	929

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

reference range so that they can determine whether or not other people have been exposed to higher levels of pirimiphos-methyl than levels found in the general population.

Table 281. 2-(Diethylamino)-6-methylpyrimidin-4-ol/one (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 2001-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	01-02	*	< LOD	< LOD	< LOD	.778 (.700-.933)	2481
Age group							
6-11 years	01-02	*	< LOD	< LOD	.680 (.560-.953)	1.17 (.737-1.27)	567
12-19 years	01-02	*	< LOD	< LOD	< LOD	.667 (.467-1.31)	810
20-59 years	01-02	*	< LOD	< LOD	< LOD	.764 (.667-.875)	1104
Gender							
Males	01-02	*	< LOD	< LOD	< LOD	.732 (.572-.986)	1165
Females	01-02	*	< LOD	< LOD	< LOD	.778 (.667-1.00)	1316
Race/ethnicity							
Mexican Americans	01-02	*	< LOD	< LOD	< LOD	.778 (.556-1.21)	669
Non-Hispanic blacks	01-02	*	< LOD	< LOD	< LOD	< LOD	687
Non-Hispanic whites	01-02	*	< LOD	< LOD	< LOD	.778 (.700-.933)	929

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

3-Chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol

Metabolite of Coumaphos

CAS No.56-72-4

General Information

The chemical 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol is a specific metabolite of coumaphos. Coumaphos is an organophosphate insecticide that is used to control insects on beef cattle, dairy cows, swine, and certain other farm animals. It is not registered for residential use in the United States.

Coumaphos and other organophosphate pesticides share a common mechanism of toxicity, inhibiting the activity of acetylcholinesterase enzymes in the nervous system. Coumaphos is considered to be an organophosphate of moderate-to-high acute toxicity. Its metabolite, 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol, does not inhibit acetylcholinesterase enzymes.

Interpreting Levels of 3-Chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol Reported in the Tables

Urinary levels of 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol were measured in a subsample of NHANES participants aged 6 years and older.

Participants were selected within the specified age range

to be a representative sample of the U.S. population. In the NHANES 2001-2002 subsample, urinary levels of 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol were below the limit of detection. In a previous nonrandom study of urine specimens obtained from adults and children in the United States, Olsson et al. (2003) found that levels of 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol were also below the limit of detection.

Finding a measurable amount of 3-chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol in urine does not mean that the level will result in an adverse health effect. These data will help scientists plan and conduct research about the relation between exposure to coumaphos and health effects. These data also provide physicians with a reference range so that they can determine whether or not other people have been exposed to higher levels of coumaphos than levels found in the general population.

Table 282. 3-Chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol

Geometric mean and selected percentiles of urine concentrations (in µg/L) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 2001-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	01-02	*	< LOD	< LOD	< LOD	< LOD	2481
Age group							
6-11 years	01-02	*	< LOD	< LOD	< LOD	< LOD	567
12-19 years	01-02	*	< LOD	< LOD	< LOD	< LOD	815
20-59 years	01-02	*	< LOD	< LOD	< LOD	< LOD	1099
Gender							
Males	01-02	*	< LOD	< LOD	< LOD	< LOD	1169
Females	01-02	*	< LOD	< LOD	< LOD	< LOD	1312
Race/ethnicity							
Mexican Americans	01-02	*	< LOD	< LOD	< LOD	< LOD	659
Non-Hispanic blacks	01-02	*	< LOD	< LOD	< LOD	.200 (<LOD-.270)	701
Non-Hispanic whites	01-02	*	< LOD	< LOD	< LOD	< LOD	920

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Table 283. 3-Chloro-7-hydroxy-4-methyl-2H-chromen-2-one/ol (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 2001-2002.

	Survey years	Geometric mean (95% conf. interval)	Selected percentiles (95% confidence interval)				Sample size
			50th	75th	90th	95th	
Total, age 6 and older	01-02	*	< LOD	< LOD	< LOD	< LOD	2480
Age group							
6-11 years	01-02	*	< LOD	< LOD	< LOD	< LOD	567
12-19 years	01-02	*	< LOD	< LOD	< LOD	< LOD	814
20-59 years	01-02	*	< LOD	< LOD	< LOD	< LOD	1099
Gender							
Males	01-02	*	< LOD	< LOD	< LOD	< LOD	1169
Females	01-02	*	< LOD	< LOD	< LOD	< LOD	1311
Race/ethnicity							
Mexican Americans	01-02	*	< LOD	< LOD	< LOD	< LOD	659
Non-Hispanic blacks	01-02	*	< LOD	< LOD	< LOD	.373 (.255-.560)	700
Non-Hispanic whites	01-02	*	< LOD	< LOD	< LOD	< LOD	920

< LOD means less than the limit of detection, which may vary for some chemicals by year and by individual sample. See Appendix A for LODs.

* Not calculated. Proportion of results below limit of detection was too high to provide a valid result.

Results by Chemical Group

Herbicides

