

Organic Mercury

TEACH Chemical Summary

Organic mercury is one of three forms of mercury listed in TEACH. In addition to this Chemical Summary, there are separate Chemical Summaries for inorganic mercury and for elemental mercury.



U.S. EPA, Toxicity and Exposure Assessment for Children's Health

This TEACH Chemical Summary is a compilation of information derived primarily from U.S. EPA and ATSDR resources, and the TEACH Database. The TEACH Database contains summaries of research studies pertaining to developmental exposure and/or health effects for each chemical or chemical group. TEACH does not perform any evaluation of the validity or quality of these research studies. Research studies that are specific for adults are not included in the TEACH Database, and typically are not described in the TEACH Chemical Summary.

I. INTRODUCTION

Mercury in elemental form is a silver-colored metal that exists as a thick liquid at room temperature, familiar to most people as the silver liquid inside mercury thermometers. Mercury can chemically combine with other elements to form organic (carbon-containing) and inorganic (not containing carbon) compounds. Mercury is a naturally-occurring metal that is also used in man-made products and processes, and is emitted into air from industrial sources (1-4). Human exposure to mercury occurs from a variety of sources, e.g., breathing mercury-containing air, using commercial products that contain mercury, and ingesting fish that contain methylmercury (1, 2, 4). The U.S. EPA provides a Web site with information about mercury exposure and effects, with a portal at www.epa.gov/mercury.

There are three major forms of mercury, each of which is covered in a separate TEACH Chemical Summary: 1) organic mercury, predominantly methylmercury found in some foods such as fish, ethylmercury found in some vaccine preservatives and some antiseptics, and phenylmercuric acetate (PMA) formerly used in some indoor paint; 2) non-elemental forms of inorganic mercury, found primarily in batteries, some disinfectants, and some health remedies and creams; and 3) elemental mercury, found in thermometers, fluorescent bulbs, dental amalgam fillings, and other sources (1, 2, 4). This TEACH Chemical Summary focuses on methylmercury, ethylmercury, and PMA. Additional information on elemental and inorganic mercury is available in their respective Chemical Summaries on the U.S. EPA TEACH Web site.

Methylmercury is commonly found in fresh or salt water fish as a result of bioaccumulation (increasing concentrations in tissues over time). Methylmercury occurs in varying amounts depending on the type of fish, with higher concentrations of methylmercury typically found in larger fish that are higher up on the food chain, particularly shark, swordfish, and tilefish (1). For methylmercury, exposure of children can occur via transfer from maternal circulation during pregnancy (i.e., *in utero*), through transfer from the mother in breast milk during lactation, or directly from children eating fish containing higher concentrations of methylmercury (1, 5).

To limit maternal and child exposures to methylmercury, the U.S. EPA and FDA jointly recommend that children, pregnant women, women who are nursing infants, and women who might become pregnant avoid eating fish with higher mercury concentrations (e.g., shark, swordfish, King Mackerel, and tilefish) (<http://www.cfsan.fda.gov/~dms/admehg3.html>) (6, 7). Also, the recommendations suggest a limit of 2 average meals per week of types of fish with lower mercury concentrations (e.g., shrimp, canned light tuna, salmon, pollock, and catfish) (6, 7). Sport fishers who eat the fish they catch can check for local state fish advisories pertaining to contaminant levels in local fish (8).

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Supporting references and summaries are provided in the TEACH Database: <http://www.epa.gov/teach>.
Document last revised 10/29/2007: includes research articles and other information through 2006.

Ethylmercury is a metabolite of thimerosal (ethyl(2-mercaptobenzoato-(2)-O,S), which is a mercury-containing chemical used as a preservative in some vaccines (1, 4, 5, 9-16). For ethylmercury, the exposure pathway of concern to children has been via vaccines; however, its use in pediatric vaccines is nearly completely phased out (10) (see Section V, Considerations for Decision Makers). The U.S. FDA regulates thimerosal use, and provides a Web site devoted to providing information regarding the use and safety of thimerosal in vaccines (<http://www.fda.gov/cber/vaccine/thimerosal.htm>) (10).

Phenylmercuric acetate (PMA) is an anti-fungal agent that had been added to interior house paint prior to 1991, at which time its use in paint was cancelled (1, 4). PMA was previously used in some pesticides, but all registered uses of PMA and other mercury-containing pesticides have been cancelled in the U.S. (4, 17, 18). Few reports are available on PMA toxicity, though kidney toxicity in adults rats has been reported (19).

The most sensitive target of organic mercury exposure, particularly methylmercury, is the nervous system (1, 2, 5, 11). In children, methylmercury exposure during pregnancy (*in utero*) has been associated with delays in reaching developmental milestones (e.g., age at first walking) and decreases in intelligence, with increasing severity with increasing exposure. At high doses of methylmercury exposure, children may experience mental retardation, reduced muscle coordination, blindness, seizures, muscle weakness, and an inability to speak (1, 2, 5, 11).

II. EXPOSURE MEDIA AND POTENTIAL FOR CHILDREN'S EXPOSURE¹

Exposure Media	Relative Potential for Children's Exposure ^{2,3}	Basis ⁴
Diet	Higher	Methylmercury bioaccumulates in the food chain, particularly in fish. Consumption of fish is the major exposure pathway for methylmercury, and concentrations vary depending on the type of fish. Methyl- and ethylmercury have been used previously as fungicides on seeds used for growing crops, but such use is currently cancelled in the U.S. and subject to severe regulatory restriction worldwide.
Medical	Lower	Thimerosal, which contains mercury, has been used previously as a preservative in some vaccines. Currently nearly all childhood vaccines are free of thimerosal or contain trace amounts (1 µg or less of mercury) with the exception being inactivated influenza (flu) vaccine; limited amounts of preservative-free flu vaccine (containing trace amounts of thimerosal) are available (http://www.fda.gov/cber/vaccine/thimerosal.htm). <i>See the Inorganic Mercury Chemical Summary for information about inorganic mercury exposure from some medicinal remedies.</i>
Ambient Air	Lower	Organic mercury is not generally found at elevated levels in ambient air.
Indoor Air	Lower	Organic mercury is not generally found at elevated levels in indoor air. <i>See the Elemental Mercury Chemical Summary for information about mercury exposure in indoor air from elemental mercury spills, such as from mercury-containing thermometer or equipment breakage.</i>
Drinking Water	Lower	Organic mercury is not generally found at elevated levels in drinking water.
Surface Water	Lower	Organic mercury is not generally found at elevated levels in surface water.
Sediment	Lower	Methylmercury persists in sediment, but is not a likely media of exposure for children.
Soil	Lower	Organic mercury is not generally found at elevated levels in soil.

¹ For more information about child-specific exposure factors, please refer to the Child-Specific Exposure Factors Handbook (<http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145>).

² The Relative Potential for Children's Exposure category reflects a judgment by the TEACH Workgroup, U.S. EPA, that incorporates potential exposure pathways, frequency of exposure, level of exposure, and current state of knowledge. Site-specific conditions may vary and influence the relative potential for exposure. For more information on how these determinations were made, go to http://www.epa.gov/teach/teachprotocols_chemsumm.html.

³ Childhood represents a lifestage rather than a subpopulation, the distinction being that a subpopulation refers to a portion of the population, whereas a lifestage is inclusive of the entire population.

⁴ Information described in this column was derived from several resources (e.g., 1-5) including studies listed in the TEACH Database (<http://www.epa.gov/teach>).

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III. TOXICITY SUMMARY^{5, 6}

Methylmercury

Methylmercury is a neurotoxicant, and may affect many areas of the brain (1, 5, 11). Reported neurotoxic symptoms of chronic methylmercury exposure include poor performance on neurobehavioral tests, particularly on tests of attention, fine motor function, language, visual-spatial abilities (e.g., drawing), and verbal memory (1, 5). Studies of neurological impairments in children who were prenatally exposed to methylmercury form the basis for the U.S. EPA Reference Dose (RfD) (1, 5). Studies have reported an association between chronic adult exposure to methylmercury and increased blood pressure, increased risk of acute myocardial infarction (heart attack), heart palpitations, hand tremors, impaired hearing, dizziness, and staggering (1, 5).

More severe symptoms have been reported following maternal acute exposure to methylmercury from poisoning incidents during pregnancy, including mental retardation, cerebral palsy, deafness, blindness, and motor impairments in their children (1, 5). Children and adults exposed to high levels of mercury, including methylmercury, have been reported to develop a disorder called acrodynia, or pink disease (1, 5, 11). Symptoms include leg cramps, irritability, redness and peeling of skin of hands, nose, and soles of the feet. Itching, fever, sweating, salivating, rashes, sleeplessness, and/or weakness have also been present. Neurological tics (involuntary muscle movements) were reported in a mercury-exposed child (20). Effects of mercury exposure in adult humans include kidney damage, and digestive tract problems including diarrhea, nausea, and ulcers (1, 5).

Ethylmercury

It has been suggested that there may be neurological effects of ethylmercury exposure from use of thimerosal in vaccines, though studies have reported conflicting results (21-26). Ethylmercury exposure from thimerosal in some vaccines has been associated, in some studies (27-33) and not others (34-40), with autism and other neurological disorders in children. Several scientific and public policy review committees carefully evaluated the data and concluded that there was not sufficient evidence of a link between autism and thimerosal in vaccines (10, 23, 24, 41). In fact, the Institute of Medicine's 2004 evaluation included an even stronger statement that rejected the idea that thimerosal-containing vaccines cause autism, concluding that "...epidemiological evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism" (16, 24).

Weighing available information with public health concerns, the American Academy of Pediatrics and the U.S. Public Health Service recommended that thimerosal be phased out of vaccines beginning in 1999 (23) (see Considerations for Decision-Makers in this Chemical Summary). Currently all routinely recommended vaccines for infants in the U.S. (except for inactivated influenza flu vaccines) are available as thimerosal-free preparations, or contain trace (very small) amounts of thimerosal (less than 1 µg mercury/dose) (<http://www.fda.gov/cber/vaccine/thimerosal.htm>) (10).

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⁵ Please refer to research article summaries listed in the TEACH Database for details about study design considerations (e.g., dose, sample size, exposure measurements).

⁶ This toxicity summary is likely to include information from workplace or other studies of mature (adult) humans or experimental animals if child-specific information is lacking for the chemical of interest. Summaries of articles focusing solely on adults are not listed in the TEACH Database because the TEACH Database contains summaries of articles pertaining to developing organisms.

Phenylmercuric Acetate (PMA)

There are few reports of health effects of PMA exposure, likely due in part to greatly reduced use of this and other mercury compounds in consumer products (42). Toxicity studies revealed kidney toxicity (19). A single case of acrodynia in a child was attributed to paint containing PMA (43), which led to a Michigan exposure study that reported higher urinary mercury concentrations in residents of homes painted with PMA-containing paint, as compared to residents in control homes (44).

Carcinogenicity Weight-of-Evidence Classification⁷: Methylmercury was classified by the U.S. EPA as class C, possible human carcinogen, based on insufficient data in humans and limited evidence of carcinogenicity in animals (www.epa.gov/iris/subst/0073.htm, II.A.1). The World Health Organization (WHO) International Agency for Research on Cancer (IARC) classified methylmercury compounds as Group 2B, “possibly carcinogenic to humans,” with inadequate evidence for carcinogenicity in humans, and sufficient evidence for carcinogenicity in experimental animals (<http://monographs.iarc.fr/ENG/Monographs/vol58/volume58.pdf>).

Ethylmercury and PMA (<http://www.epa.gov/iris/subst/0089.htm>) have not been evaluated for carcinogenicity by the U.S. EPA, or by the WHO IARC (<http://monographs.iarc.fr/ENG/Classification/Listagentsalphorder.pdf>).

IV. EXPOSURE AND TOXICITY STUDIES FROM THE TEACH DATABASE

This section provides a brief description of human and animal studies listed in the TEACH Database. For more details about study design parameters, e.g., doses and exposure information, please refer to article summaries in the TEACH Database. Any consideration should include an understanding that exposure levels in animal studies, in many cases, are greater than exposure levels normally encountered by humans.

A. HUMAN EXPOSURE AND EFFECTS

Studies that measured total mercury, without distinguishing forms of mercury:

- ▶ Total mercury has been measured in many types of food (1, 4, 45-47), including infant and toddler foods (45) and children’s diet (47). Another study estimated mercury exposure of children from diet in Canada (46). The largest proportion of mercury in diet was attributed to the presence of methylmercury in fish (1).
- ▶ Total mercury concentrations have been measured in fetal cord blood (48-53), placenta (49, 50), and fetal hair (50). One study in Tennessee measured total mercury in fetal blood, placenta, and maternal blood for over 650 pregnancies, and reported significant correlations between mercury concentrations in maternal blood and in fetal blood (50). In another study, mercury concentrations in cord blood were not correlated with the distance of these mother’s homes from an industrial area (48).

⁷ For recent information pertaining to carcinogen risk assessment during development, consult Guidelines for Carcinogen Risk Assessment and Supplemental Guidance on Risks from Early Life Exposure at <http://www.epa.gov/cancerguidelines>.

- ▶ Total mercury concentrations have also been measured in blood, urine, fingernails, and hair of children (21, 52, 54-77), as well as in breast milk (49, 52, 78-85). Also, as part of an ongoing large national study (National Health and Nutrition Examination Survey, or NHANES; 1999-2002), total mercury concentrations were measured in blood of children 1-5 years old, and in blood and urine of women 16-49 years old (58). Results indicated that 5.7% of women 16-49 years old had mean total mercury concentrations in blood higher than 5.8 µg/L (blood mercury levels below 5.8 µg/L, the U.S. EPA reference blood level, were estimated to be without appreciable harm) (68).
- ▶ Possible effects from mercury exposure on pregnancy outcome have been studied. One study found an association between increased incidence of miscarriage and total mercury concentrations in well water (86). In a study of pregnant women in Iowa, increasing blood total mercury concentrations were correlated with the incidence of previous stillbirths, and separately with a history of having children with birth defects (87).
- ▶ Longitudinal studies (which follow subjects over time) of possible neurodevelopmental effects of mercury exposure have been performed, measuring total mercury concentrations in hair and blood of pregnant women and their children over time (1, 88). In studies from the Faroe Islands and elsewhere, poorer performance on neuropsychological tests in children was associated with higher concentrations of mercury in maternal hair during pregnancy or in cord blood (51, 69, 89-97). Similar correlations were found in another study in New Zealand (98). In contrast, other studies in the Seychelles Islands found few correlations between mercury concentrations in maternal hair and neurological impairments in children (99-110). Mercury exposures in the studies cited above were largely attributed to methylmercury exposure from the consumption of fish in the diet (5, 89-91, 99-108, 111-113). These large studies, in conjunction with other data, have been carefully evaluated and analyzed by the National Research Council and the U.S. EPA, and provide the basis for derivation of the current U.S. EPA oral reference dose (RfD) for methylmercury (5, 113, 114).
- ▶ Children's total mercury blood concentrations were significantly associated with other health effects, including increased N-acetyl-beta-D glucosaminidase (a measure of kidney function) and decreased serum prolactin (indicating a shift in neurobiochemical metabolism) (74). Total mercury concentrations in blood and in hair were significantly associated with decreased logical and spatial abilities (72). There were no significant impairments in cognitive testing of children with amalgam (mercury-containing) dental fillings, as compared to children with composite (mercury-free) fillings (115, 116). More information about mercury exposure from dental amalgam use is summarized in the TEACH Elemental Mercury Chemical Summary.
- ▶ Possible associations between autism spectrum disorders (ASD) and environmental exposure to mercury have been explored. Increased incidence of ASD was associated with mercury air concentration at the census tract level (117), and with total reported environmental mercury releases (118). One study reported no significant difference in blood concentrations of total mercury between children with ASD, and children without ASD (119).
- ▶ Some adverse effects on vision (e.g., reduced contrast sensitivity, with difficulties sensing shades of gray) in children were significantly associated with increased total mercury concentrations in blood (120). In another study, there was no association between contrast sensitivity in 7 year old children, and their cord blood total mercury concentrations at birth (121).

- ▶ Increases in blood pressure and decreases in heart rate variability in 7-year-old children were associated with increasing total mercury concentrations in cord blood at their birth (122). A follow-up of those children at 14 years of age revealed that there was no longer a significant increase in blood pressure associated with cord blood mercury concentrations, though a significant association with decreases in heart rate variability remained (123).
- ▶ Exploring possible thyroid effects, one study reported no significant association between cord blood total mercury concentrations and infant thyroid hormone concentrations (53). Another large study of children found no correlation between blood total mercury levels and blood thyroid hormone levels (124).

Studies that measured methylmercury:

- ▶ Methylmercury has been shown to cross the placenta (125-128). Methylmercury has been measured in breast milk (59, 82, 129); and in blood, urine, and hair of children (21, 55, 59, 82, 130, 131). One study that included children from middle to higher income families in San Francisco found that, of 7 children tested, 4 of them had blood mercury levels (11.2-26 ug/L) that were 40 times the national average for their age group; their families reported frequent eating of fish in their diet (55).
- ▶ There are numerous studies of effects in children following exposure to low levels of organic mercury, with much of the information focused on methylmercury exposure (1, 5, 88). The primary health concern has been fetal exposure to methylmercury during pregnancy, and research results from such studies form the basis for deriving U.S. EPA toxicity values (see Section IV.A., bullet 5 in this Chemical Summary) (1, 5, 12). Recent studies reported mild-to-moderate impairments detected in visual (132) and behavioral (133) tests of children that were associated with mercury or methylmercury blood concentrations.
- ▶ Information on effects of high-dose, prenatal exposure to methylmercury was reported following two separate major poisoning incidents, one in Minamata, Japan (between 1953 and 1966) and one in Iraq (between 1955 and 1972) (1). In Japan, prenatal exposure to high levels of methylmercury via maternal fish consumption, harvested from local ocean waters contaminated with mercury, was associated with increased incidence of still births and miscarriages (134), and severe developmental disabilities and other adverse neurological effects in children born to exposed mothers (135, 136). In Iraq, prenatal exposure to high levels of methylmercury occurred via maternal consumption of contaminated grain, and resulted in diffuse central nervous system damage, disruption of neuronal cell migration, and increased incidence of adverse behavioral effects in exposed adults and offspring (137, 138).
- ▶ Other health effects in children have been reported. Children and adults exposed to methylmercury have developed a disorder called acrodynia, manifested by symptoms that include: leg cramps; irritability; redness and peeling of skin of hands, nose, and soles of the feet; itching; fever; sweating; excessive salivating; sleeplessness; photophobia; and/or weakness (1, 5). Impaired growth of children was significantly associated with maternal exposure to methylmercury during pregnancy (139).

Studies that measured ethylmercury:

- ▶ Thimerosal is a compound that contains mercury, and when metabolized in the body, forms ethylmercury (1, 4, 5, 9-15). Ethylmercury has been detected in blood, urine, and feces of infants who were vaccinated with thimerosal-containing vaccines (140, 141). Levels of mercury in blood and feces of infants who had received routine immunizations were measured, and were found to be within safety guidelines set for methylmercury exposure by the U.S. FDA, U.S. ATSDR, and World Health Organization (10, 140, 141). Mercury was excreted by thimerosal-exposed infants in blood and feces at a faster rate than expected for methylmercury, suggesting that thimerosal and methylmercury are metabolized and excreted differently (140).
- ▶ Interpretations of studies of possible links between autism in children and exposure to ethylmercury from thimerosal in vaccines have been the subject of controversy (22-26). Some studies suggested a link between ethylmercury exposure from thimerosal in some vaccines with autism and other neurological disorders in children (28-33, 142, 143), while other studies found no such association (34-40, 144). Several scientific and public policy review committees carefully evaluated available data on this issue, and concluded that the evidence suggesting a link between autism and thimerosal was not sufficient (23, 24). Weighing available information with public health concerns, the American Academy of Pediatrics and the U.S. Public Health Service recommended that thimerosal be phased out of vaccines beginning in 1999 (23) (see Considerations for Decision-Makers in this Chemical Summary).

Studies that measured phenylmercuric acetate (PMA):

- ▶ A single case of acrodynia in a child, attributed to use of house paint containing PMA (43), led to a Michigan exposure study that reported higher urinary mercury concentrations in residents of homes painted with PMA-containing paint, as compared to residents in control homes (44).

B. EXPERIMENTAL ANIMAL EXPOSURE AND EFFECTS

Numerous animal studies of adverse health effects following methylmercury and ethylmercury exposure have been performed, starting back in the mid 1950's when a link was suspected between consumption of fish and adverse health effects in adults and their offspring in Minamata, Japan. The TEACH Database does not list articles published prior to 1972. Animal studies highlighted in this section focus on studies that provide information that supplements information from human studies, pertaining to health effects of organic mercury exposure during development. Studies discussed here administered methylmercury by the oral route unless indicated otherwise.

- ▶ Uptake and tissue distribution of mercury following methylmercury exposure during development have been studied extensively. Methylmercury was shown to cross the placenta and accumulate in fetal brain, kidney, and liver in mice (145, 146), hamsters (147-149), rats (150-154), and monkeys (155). Methylmercury administered to lactating mothers was also transferred to offspring via breast milk in rats (150, 153, 156, 157) and hamsters (148, 149). Mercury was passed from mother to offspring more efficiently by placental transfer than by breast feeding in rats (153) and hamsters (148, 149).

- ▶ Clearance and metabolism of methylmercury have also been studied. A recent study showed that prenatal exposure of rats to methylmercury resulted in increased levels of mercury in brains of offspring, which remained elevated until clearance from the body by 60 days of age (adulthood) (151). Also, maternal methylmercury exposure of hamsters to methylmercury resulted in detection of inorganic mercury in fetal liver and brain, suggesting that methylmercury may be demethylated to generate inorganic mercury in the body (147, 148).
- ▶ Comparisons of methylmercury and ethylmercury tissue distribution following exposure in young mice (158) and monkeys (155) both reported significantly less mercury deposited in the brain following ethylmercury or thimerosal exposure, as compared to methylmercury exposure. Another rat study compared tissue distribution of ethylmercury and mercuric chloride injection of nursing pups, and found significant differences in mercury tissue distribution between the two forms of mercury (i.e., more mercury in kidney and liver with mercuric chloride exposure, and more mercury in blood and brain with thimerosal exposure)(159). The authors of these studies concluded that the clearance and tissue distribution of methylmercury, ethylmercury, and mercuric chloride are significantly different in each species tested (155, 158, 159). The route of exposure (injection versus ingestion) to methylmercury also resulted in differences in the amount of mercury deposited in the brain in mice, with exposure via intramuscular injection resulting in less mercury deposition than via ingestion (158).
- ▶ Some animal studies have demonstrated differences between sexes or between strains of animals in their sensitivity to the toxic effects of methylmercury exposure during prenatal development. Adult male rats, but not female rats, who were exposed *in utero* to methylmercury, had decreased motor activity (160). Young female mice demonstrated deficiencies in learning and memory tasks as adults, following juvenile exposure to methylmercury, and young male mice showed no such deficiencies (161). Differences in neurotoxicity between strains of mice have been observed following prenatal exposure to methylmercury, with a greater incidence of hydrocephaly (enlarged brain) (162), and greater deficiencies in learning tasks and memory (163) in some strains than others.
- ▶ Prenatal exposure to methylmercury has been shown to be embryotoxic and teratogenic in multiple species of animals (164). Observed defects at birth included cleft palate, hydrocephaly, and delayed ossification (hardening of bone) (154, 164, 165).
- ▶ Effects of methylmercury exposure combined with other stressors on pregnancy and development have been studied. Combined exposure to methylmercury plus lead and/or arsenic resulted in greater maternal toxicity, but not increased developmental effects on the fetuses (166). Methylmercury exposure combined with maternal stress induced by restraint also resulted in increased maternal toxicity, but little or no increased fetal developmental effects (167, 168).
- ▶ Numerous studies in mice, rats, and monkeys have focused on neurological and behavioral effects in offspring following prenatal and, to a lesser extent, early life exposure to methylmercury (169-172). Impairments were detected in visual, auditory, sensory, and neuromuscular coordination skills, though some studies detected no defects in the parameters measured.

- ▶ Persistence of neurological and behavioral effects following prenatal or lactational exposure to methylmercury was manifested in adulthood in some studies, well after exposure was stopped. Effects manifested in adulthood included learning deficits in rats (172, 173) and in monkeys (174), increased spontaneous activity in male rats (62), and hydrocephaly in mice (162). Some neurological effects of prenatal exposure to methylmercury were manifested only in adult animals and not young animals (175). Another study reported lower visual contrast sensitivity in adult monkeys (176), and auditory impairments in adult female rats (177) who were exposed to methylmercury *in utero*.
- ▶ Treatment regimens for the prevention of methylmercury-induced neurotoxicity have been explored. Some compounds have been shown to reduce the severity of adverse effects of methylmercury exposure in animal studies, including N-acetyl-L-cysteine (178), meso-2,3-dimercaptosuccinic acid (165, 179), and 2,3-dimercaptopropanol (180). However, co-administration of selenium with methylmercury led to increased accumulation of methylmercury in fetal tissues in mice (145, 146, 181).

V. CONSIDERATIONS FOR DECISION-MAKERS

This section contains information that may be useful to risk assessors, parents, caregivers, physicians, and other decision-makers who are interested in reducing the exposure and adverse health effects in children for this particular chemical. Information in this section focuses on ways to reduce exposure, assess possible exposure, and, for some chemicals, administer treatment.

Information about Reducing or Preventing Exposures to Methylmercury

- ▶ Eating seafood that contains methylmercury is a major pathway of exposure for pregnant women and children (1, 5). The amount of mercury present in fish varies depending on the type of fish. Fish higher on the food chain and larger in size are more likely to contain higher levels of mercury (7). According to joint recommendations from the U.S. EPA and the U.S. Food and Drug Administration (FDA), children, pregnant women, women who are nursing infants, and women who might become pregnant should **NOT** eat shark, tilefish, King Mackerel, and swordfish, because of high levels of mercury in these fish (7). Some fish with lower levels of methylmercury include shrimp, canned light tuna, wild salmon, and pollock, with recommended consumption of up to 2 meals per week for pregnant women and children (7). A comprehensive list of species of fish, and their measured tissue mercury levels, is available from the U.S. FDA (182).
- ▶ Sport fishers and their families, who eat the fish that they catch in local salt or fresh waters, should obtain information about local fish advisories in their state (8). Many states have local fish advisories that make recommendations for the amount of certain types of fish to consume per week, based on levels of methylmercury or polychlorinated biphenyl (PCB) contamination detected in local fish samples.

Information about Reducing or Preventing Exposures to Ethylmercury

- ▶ Most childhood vaccines currently do not contain thimerosal (10). If parents or guardians are concerned about thimerosal, ask your health care provider for specific information on whether or not the vaccines in question contain thimerosal.
- ▶ Parents and guardians are strongly urged by the American Association of Pediatrics (AAP), U.S. Public Health Service (PHS), the Centers for Disease Control (CDC), and the U.S. FDA to have their children vaccinated in order to avoid serious infectious diseases, particularly with the current status of phased-out thimerosal use in pediatric vaccines (10, 23, 24, 183).
- ▶ Currently all routinely recommended vaccines for infants in the U.S. (except for inactivated influenza flu vaccines) are available as thimerosal-free preparations, or contain trace (very small) amounts of thimerosal (less than 1 µg mercury/dose) (<http://www.fda.gov/cber/vaccine/thimerosal.htm>) (10). Ask your health care provider about thimerosal-free pediatric vaccines, including some pediatric flu vaccines (10). The use of thimerosal in vaccines has been phased out since 1999, when the AAP and the U.S. PHS recommended this action (23).
- ▶ Other preparations currently manufactured without thimerosal include all immune globulin preparations (e.g., hepatitis B immune globulin and Rho(D) immune globulin preparations), according to the FDA (10). Thimerosal was never used in some vaccines, including inactivated polio (IVP), varicella (chickenpox), pneumococcal conjugate, and the mumps/measles/rubella (MMR) vaccines, according to the CDC (10, 12). Some vaccines indicated for older children (>7 years old) and adults, such as Td, contain thimerosal and are available in preparations with little or no thimerosal (184).
- ▶ According to the Institute of Medicine (IOM), “based on [the current] body of evidence, the committee concludes that the evidence favors rejection of a causal relationship between thimerosal-containing vaccines and autism” (41). Several scientific advisory panels, including the AAP (23), the IOM (16, 24), and the U.S. FDA (10), evaluated existing studies before coming to this conclusion.
- ▶ Chelation therapy (medical treatment for clearing the body of some metals) has been pursued by some parents of children with autism as a treatment for their condition. According to the Institutes of Medicine, “The [Vaccine Safety] committee heard from some parents of children with [autism spectrum disorder (ASD)] who have chosen to rely on chelation therapy as a treatment. The committee saw no scientific evidence, however, that chelation is an effective therapy for ASD or is even indicated in these circumstances. Chelation therapy is currently indicated only for high-dose, acute mercury poisonings. Because chelation therapy has potentially serious risks, the committee recommends that it be used only in carefully controlled research settings with appropriate oversight by Institutional Review Boards protecting the interests of the children who participate” (41).
- ▶ Fact sheets for parents are available that provide information pertaining to the use of thimerosal in vaccines, and explain current recommendations (12-15, 183). A review of thimerosal information is available from the U.S. FDA, and includes list of thimerosal concentrations in specific vaccines, if present (10).

Other Information about Mercury

- ▶ Mercury exposure can occur as a consequence of spills from broken thermometers, gauges, or other commercially-available items that contain mercury (185); for more details see the TEACH Elemental Mercury Chemical Summary. Mercury exposure can also occur from use of some medicinal remedies and skin bleaching creams (185); for more details see the TEACH Inorganic Mercury Chemical Summary.
- ▶ The U.S. EPA provides a Web site with a broad array of information resources pertaining to mercury exposure and health effects (www.epa.gov/mercury). Detailed compilations and analyses of information pertaining to exposure and health effects of organic mercury are available in the ATSDR Toxicological Profile for Mercury (1); and in the more recent National Research Council (NRC) document, Toxicological Effects of Methylmercury (5). A Hazard Summary for Mercury Compounds is also available from the U.S. EPA, which summarizes information derived from several sources (186).
- ▶ A health risk assessment for mercury and mercury compounds is available as a component of a comprehensive U.S. EPA document, “Mercury Study Report to Congress,” which detailed available information about mercury emissions, health and environmental implications of those emissions, and emission control technologies (11).
- ▶ Mercury and mercury compounds are ranked as number 3 on the 2005 Priority List of Hazardous Substances for the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104 (i), as amended by the Superfund Amendments and Reauthorization Act (SARA). This is a list, in the order of priority of concern, of substances most commonly found at sites listed on the National Priorities list (NPL); there are currently 275 substances on this list (187). Mercury has been found in at least 714 of 1,467 current or former NPL sites (1). Methylmercury is ranked as number 121 on this list (187).
- ▶ The U.S. EPA used 1999 emissions data for mercury compounds for all 50 states to report county-level emissions, modeled ambient air concentration estimates, modeled human inhalation exposure, and estimated risk (188).
- ▶ Concentrations of mercury in urine and blood of women 16-49 years old, and blood of children 1-5 years old were measured from 1999-2002 as part of the ongoing National Health and Nutrition Examination Survey (NHANES) (58). This comprehensive survey is administered on an ongoing basis by the U.S. Centers for Disease Control and Prevention National Center for Health Statistics, with results reported every two years (58).
- ▶ Mercury was included in the list of chemicals measured in the National Human Exposure Assessment Survey (NHEXAS), designed to evaluate human exposure to several chemicals on a regional scale in the U.S. (189). Information on mercury levels in hair of 182 people, including children, living in the Midwest was reported as part of this survey (190).
- ▶ Consult the U.S. EPA “Child-Specific Exposure Factors Handbook” (EPA-600-P-00-002B) for factors to assess children’s ingestion rates (191). An updated External Draft of the 2006 version of this handbook is available (192).

VI. TOXICITY REFERENCE VALUES

Methylmercury

A. Oral/Ingestion

U.S. EPA Reference Dose (RfD) for Chronic Oral Exposure: 1E-4 (or 0.0001) mg/kg-day; based on developmental neuropsychological impairment from epidemiological studies in humans (www.epa.gov/iris/subst/0073.htm, I.A.1) (114). Last Agency Consensus Date 6/19/01.

ATSDR Minimal Risk Level (MRL): Chronic oral (developmental endpoint), 0.0003 mg/kg/day. (www.atsdr.cdc.gov/mrls.html) (193). Last revised 3/99.

Ethylmercury

No toxicity reference values available.

Phenylmercuric Acetate

C. Oral/Ingestion

U.S. EPA Reference Dose (RfD) for Chronic Oral Exposure: 8E-5 (or 0.00005) mg/kg-day; based on renal damage in rat oral chronic study (<http://www.epa.gov/iris/subst/0089.htm>, I.A.1) (19). Last Agency Verification Date 8/19/85.

VII. U.S. FEDERAL REGULATORY INFORMATION

- ▶ Mercury is one of 188 hazardous air pollutants (HAPs) listed under section 112(b) of the 1990 Clean Air Act Amendments and is regulated from more than 170 industrial source categories (194).
- ▶ The U.S. EPA has set an Ambient Water Quality Criterion that protects human health by setting an acceptable level of methylmercury in the tissue of fish, defined as a Tissue Residue Criterion, rather than in the water. The U.S. EPA concluded that levels of methylmercury in fish were most relevant to protecting public health, because it is the fish consumed by humans that is the major route of methylmercury exposure. Exposure of humans to methylmercury via water was determined to be negligible. The Tissue Residue Criterion is 0.3 mg methylmercury/kg fish (195). The U.S. FDA also sets tolerances for methylmercury in fish, which includes commercially-sold fish (196).
- ▶ The U.S. EPA has cancelled ethylmercury and methylmercury uses as a fungicide on food grain in the U.S., and such use is discouraged worldwide by the World Health Organization (1, 197).
- ▶ Use of phenylmercuric acetate (PMA) in paint has been cancelled since 1991 (1).

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- ▶ The U.S. EPA requires reporting of quantities of certain chemicals that exceed a defined reportable quantity, and that quantity varies for different chemicals (198). Mercury is classified under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 “Toxic Chemicals” as a persistent, bioaccumulative and toxic compound (PBT) and as such, reporting quantities of mercury greater than 10 pounds manufactured or processed, or otherwise used, is required. Under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), reporting mercury releases of any quantity exceeding 1 pound is required. PMA is classified as an “Extremely Hazardous Substances” (EHS); PMA is listed under EPCRA section 302 (Threshold Planning Quantity=500 pounds processed, or 100,000 otherwise released), section 304 (Reportable Quantity=100 pounds); section 313c (listed under multiple categories, i.e. mercury compounds), and CERCLA (Reportable Quantity=100 pounds). Under CERCLA, PMA is listed on the P list (P092) (198).
- ▶ For a comprehensive list of mercury regulations and standards, go to <http://www.epa.gov/mercury/regs.htm>.

VIII. BACKGROUND ON CHEMICAL

Methylmercury

A. CAS Number: 022967-92-6

B. Physicochemical Properties: Methylmercury is a compound that bioaccumulates in living organisms, especially fish, following exposure to mercury; ethylmercury is generated in the body after metabolism of thimerosal. Go to the National Library of Medicine ChemID Web site (<http://chem.sis.nlm.nih.gov/chemidplus>) and search for methylmercury or thimerosal. Ethylmercury is not listed at this Web site.

C. Production: Methylmercury is not produced in man-made processes, but is generated in the environment by conversion of inorganic and elemental mercury in living organisms. Methylmercury is found in the tissues of organisms, particularly fish and ocean mammals (1, 4, 195, 197). Methylmercury may be found in water and soil as the result of the methylation of elemental and inorganic mercury by microorganisms (1, 4, 195, 197). Most of the mercury found in the environment is elemental and inorganic mercury, released into air from mercury mining processes, emissions of coal-fired power plants, emissions from some solid waste incinerators, and other industrial sources (1, 4, 195, 197). A recent analysis estimated that U.S. production of total mercury from secondary facilities is approximately 430 tons/year (199).

D. Uses: There are no known uses for methylmercury. Thimerosal contains mercury and is metabolized in the body to form ethylmercury; thimerosal has been used as a preservative in some vaccines, though such pediatric uses are uncommon and continue to be phased out. PMA was used in paints as a mold preventative, but its use has been cancelled since 1991 (1). In 2004, the total amount of TRI-reported releases and disposals of mercury compounds in the U.S. was over 4.7 million pounds; total releases are likely to be greater than this estimate because not all sources of mercury compound releases are required to report (200).

E. Environmental Fate: Mercury is a naturally-occurring element. Mercury is present in the environment as a result of both natural and human activities. Mercury persists in the environment, though the form in which it exists changes over time (1, 21, 201). Metallic mercury enters the air from mining ore deposits, burning coal and waste, and from manufacturing plants (1, 21). It enters the water or soil from erosion of natural deposits, discharge from refineries and factories, and runoffs from landfills and crop lands. Mercury emissions are transported through ambient air, and deposited to water and land where humans and wildlife can be exposed. Mercury concentrations in ambient air are usually low (1, 21). Once mercury enters water, either through air deposition or soil runoff, microorganisms such as bacteria transform inorganic mercury in the environment to methylmercury, which can then bioaccumulate in fish and animal tissue (1). Some types of fish (e.g., shark, swordfish, and tile fish) have higher levels of methylmercury than others (8, 182, 201-203). If elemental mercury is spilled or released indoors, it can volatilize into the air and be redeposited, remaining in homes for many years if not cleaned up properly (see the TEACH Elemental Mercury Chemical Summary) (1, 204).

F. Synonyms: methylmercury (I) ion, methylmercury (II) cation, methyl mercury, ethyl mercury.

Additional information on methylmercury, ethylmercury, and PMA is available in the TEACH Database for Organic Mercury, and at the following Web sites:

www.epa.gov/mercury/

www.epa.gov/glnpo/sediments.html

www.epa.gov/ost/fish/mercurydata.html

www.epa.gov/grtlakes/bnsdocs/hg/hgbrief.html

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