TOXICOLOGICAL PROFILE FOR MERCURY (UPDATE)
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY
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EXCERPTS REGARDING THE HEALTH HAZARDS OF MERCURY AMALGAM FILLINGS:

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Mercury is mined as cinnabar ore, which contains mercuric sulfide. **Silver-colored dental fillings typically contain about 50% metallic mercury.** These uses may pose a health risk from exposure to mercury both for the user and for other whom may be exposed to mercury vapors in contaminated air.

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A potential source of exposure to metallic mercury for the general population is mercury released form dental amalgam fillings. The amalgam used in silver-colored dental fillings contains approximately 50% metallic mercury, 35% silver, 9% tin, 6% copper, and trace amounts of zinc. Very small amounts are slowly released from the surface of the filling due to corrosion or chewing or grinding motions. Part of the mercury at the surface of the filling may enter the air as mercury vapor or be dissolved in the saliva. The total amount of mercury released from dental amalgam depends upon the total number of fillings and surface of each filling. Estimates of the amount of mercury released from dental amalgams range from 3 to 17 micrograms per day (hg/day). The mercury from dental amalgam may contribute from 0 to more than 75% of your total daily mercury exposure. Sensitive populations may include pregnant women; children under the age of 6 (especially up to the age of 3), people with impaired kidney function, and people with hypersensitive immune responses to metals.

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Workers are mostly exposed from breathing air that contains mercury vapors, but may also be exposed to other inorganic mercury compounds in the workplace. Occupations that have a greater potential for mercury exposure include the medical professions (medical, dental, or other health services) where equipment may contain mercury (e.g., some devices that measure blood pressure contain liquid mercury). **Dentists and their assistants may be exposed to metallic mercury from breathing in mercury vapor released from amalgam fillings and to a much lesser extent from skin contact with amalgam restorations.** Family members of workers who have been exposed to mercury may also be exposed to mercury if the worker's clothes are contaminated with mercury particles of liquid.

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Inorganic mercury accumulates mostly in the kidneys and does not enter the brain as easily as metallic mercury. Inorganic mercury compounds also do not move as easily from the blood of a pregnant woman to her developing child. In a nursing woman, some of the inorganic mercury in her body will pass into her breast milk. Once organic mercury is in the blood stream, it moves easily to most tissues and readily enters the brain. **Methylmercury that is in the blood of a pregnant woman will easily move into the blood of the developing child and then into the child's brain and other tissues.** Like metallic mercury, methylmercury can remain there for a long time. When methymercury does leave your body after you have been exposed, it leaves slowly over a period of several months, mostly as inorganic mercury in the feces. **As with inorganic mercury, some of the methylmercury in a nursing woman's body will pass into her breast milk. The nervous system is very sensitive to mercury.**

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Permanent damage to the brain has also been shown to occur from exposure to sufficiently high levels of metallic mercury. Whether exposure to inorganic mercury results in brain or nerve damage is not as certain, since it does not easily pass from the blood into the brain. **Metallic mercury vapors or organic mercury may affect many different areas of the brain and their associated functions, resulting in a variety of symptoms, including personality changes (irritability, shyness, nervousness), tremors, changes in vision (constriction (or narrowing) of the visual field), deafness, muscle incoordination, loss of sensation,**

and difficulties with memory. When metallic mercury vapors are inhaled, they readily enter the bloodstream and are carried throughout the body and can move into the brain. Breathing in or swallowing large amounts of methylmercury also results in some of the mercury moving into the brain and affection the nervous system. All forms of mercury can cause kidney damage if large enough amounts enter the body. Short-term exposure (hours) to high levels of metallic mercury vapor in the air can damage the lining of the mouth and irritate the lungs and airways, causing tightness of the breath, a burning sensation in the lungs, and coughing. Damage to the lining of the mouth and lungs can also occur from exposure to lower levels of mercury vapor over periods (for example, in some occupations where workers were exposed to mercury for many years).

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The Environmental Protection Agency has determined that mercury chloride and methylmercury are possible human carcinogens.

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Inorganic mercury and methylmercury can also pass from a mother's body into breast milk and into a nursing infant. Methylmercury can also accumulate in an unborn baby's blood to a concentration higher than the concentration in the mother. High exposure to mercury vapor causes lung, stomach, and intestinal damage and death due to respiratory failure in sever cases. These effects are similar to those seen in adult groups exposed to inhaled metallic mercury vapors at work. Kidney damage is very common after exposure to toxic levels of inorganic mercury. Metallic mercury or methylmercury that enters the body can also be converted to inorganic mercury and result in kidney damage. In critical periods of development before they are born, and in the early months after birth, children and fetuses are particularly sensitive to the harmful effects of metallic mercury and methylmercury on the nervous system.

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One way in which people are routinely exposed to extremely small amounts of mercury is through the gradual (but extremely slow) wearing-away process of dental amalgam fillings, which contain approximately 50% mercury. The amount of mercury to which a person might be exposed from dental amalgams would depend on the number of amalgams present and other factors.

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The general population is most commonly exposed to mercury primarily from two sources: eating fish and marine mammals or from the release of elemental mercury from the dental amalgams used in fillings.

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At high exposure levels, respiratory, cardiovascular, and gastrointestinal effects also occur. Some metallic mercury **vapor may condense (Milne et al.1970), or in the case of vapors from dental amalgam, may dissolve in saliva and be ingested (WHO 1991).**

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Metallic Mercury
Several studies have reported death in humans following accidental acute-duration exposure to high, but unspecified, concentrations of metallic mercury vapor. (Campbell 1948;Kanluen and Gottlieb 1991;Matthes et al. 1958; Rowens et al. 1991; Soni et al, 1992; Taueg et al. 1992; Teng and Brennan 1959; Tennant et al. 1961).

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Metallic Mercury
In humans, respiratory symptoms are a prominent effect of acute-duration high-level exposure to metallic mercury vapors. The most commonly reported symptoms include cough, dyspnea, and tightness of burning pains in the chest (Bluhm et al. 1992a; Gore and Harding 1987; Haddad and Sternberg 1963; Hallee 1969; Kanluen and Gottlieb 1991; King 1954; Lilis et al. 1985 Matthes et al. 1958; McFarland and Reigel 1978; Milne et al. 1970; Rowwens et al. 1991; Snodgrass et al. 1981; Soni et al. 19912; Taueg et al. 1992; Teng and Brennan 1959; Tennant et al 1961).

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Dentists (n=98, mean age 32, range 24-49) with an average of 5.5 years of exposure to low levels of mercury showed impaired performance on several

neurobehavioral tests (Ngim et al. 1992). Controls were matched for age, fish consumption, and number of amalgam fillings. The dentists had a higher aggression score than the controls. In a study of the relation between cumulative exposure to mercury and chronic health impairment, 298 dentists had their mercury levels measured by an x-ray fluorescence technique. Electrodiagnostic and neuropsychological findings in the dentists with more than 20hg/g tissue (head and wrist) mercury levels were compared with a control group consisting of dentists with no detectable mercury levels. 23 of the 298 dentists with the highest mercury levels were administered neurological tests and compared to the controls. The high mercury group had slowed conduction velocities in motor (median nerve) and sensory (suralnerve) nerves, mild neuropsychological impairment (increased errors in the Bender-Gestalt test), mild visuographic dysfunction, and higher distress levels (self-reported) than the control group. Seven of the high exposure dentists showed manifestations of polyneropathy. No polyneuropathies were detected in the control group (Shapiro et al. 1982).

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The primary pathways of mercury exposure for the general population are from eating fish or marine mammals that contain methylmercury, **or from breathing in or swallowing very small amounts of mercury that are released from the dental amalgam used for fillings.** The relative contribution of mercury from these two main sources will vary considerably for different individuals, depending upon the amount of fish consumed, the level of mercury in the fish, the number of amalgam fillings, eating and chewing habits, and a number of other factors.

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Dental amalgams, however, would be the most significant source of mercury exposure in the absence of fish consumption or proximity to a waste site or incinerator. A report from the Committee to Coordinate Environmental Health and Related Programs (CCEHRP) of the Department of Health and Human Services determined a level of from 1to 5 hg Hg/day from dental amalgam for the people with 7-10 fillings (DHHS 1993) The World Health Organization reported a consensus average estimate of 10 hg amalgam Hg/day (range: 3-17 hg/day) (WHO 1991). Weiner and Nylander (1995) estimated the average uptake of mercury from amalgam fillings in Swedish subjects to be within the range of 4-19 hg/day. Skare and Engqvist (1994) estimated that the systemic uptake of mercury from amalgams in middle -aged Swedish individuals with a moderate amalgam load (30 surfaces) was, on the average, 12 hg/day, an amount said to be equivalent to a daily occupational air mercury exposure concentration of 2 hg/day. Other researchers have estimated the average daily absorption of Hg from amalgam at 1-27 hg/day, with levels for some individuals being as high as 100 hg/day (Bjorkman et al. 1997; Lorscheider et al. 1995).

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Systemic Effects - Respiratory Effects
The evidence from case report studies suggests that inhalation of metallic mercury vapor may result in clinical respiratory symptoms (e.g., chest pains, dyspena, cough, reduced vital capacity) (Bluhm et al. 1992a; Gore and Harding 1987; Haddad and Stern 1963; Hallee1969; Kanluen and Gottlieb 1991; King 1954; Lilis et al. 1985; Matthes et al. 1958; McFarland and Reigel 1978; Milne et al.1970; Rowens et al. 1991; Snodgrass et al. 1981; Soni et al. 1992; Taueg et al. 1992; Teng and Brennan 1959; Tennant et al. 1961). In the more severe cases, respiratory distress, pulmonary edema, lobar pneumonia, fibrosis, desquamation of the bronchiolar epithelium, and death due to respiratory failure have been observed (Campbell 1948; Gore and Harding 1987; Jaffe et al. 1983; Kanluen and Gottlieb 1991; Matthes et al. 1958; Taueg et al. 1992; Teng and Brennan 1959; Tennant et al. 1961).

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Of particular interest is the study showing slightly higher blood pressure in persons with dental amalgams than in those with no mercury-containing amalgams (Siblerud 1990).

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Irritation of the oral mucosa has also been observed at the site of contact with dental amalgams that contain mercury (Veien 1990).

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Renal effects
The kidney is one of the major target organs of mercury-induced toxicity. Adverse renal effects have been reported following exposure to metallic, inorganic, and organic forms of mercury in both humans and animals.

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Immunological Effects.
As indicated in the section on dermal effects, allergic dermatological reactions occurred in persons exposed to inorganic mercury from dental amalgams, tattoos, or breakage of medical instruments (Anneroth et al. 1992; Bagley et al. 1987; Biro and Klein 1967; Faria and Freitas 1992; Goh and Ng 1988 ; Pambor and Timmel 1989; Skoglund and Egelrud 1991; Veien 1990). Additionally, **mercury may cause either decreases in immune activity or an autoimmune response, depending on the genetic predisposition of the individual exposed.**

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Neurological Effects.
The nervous system is the primary target organ for elemental and methylmercury - induced toxicity. Autopsy findings of degenerative changes in the brains of poisoned patients exposed to mercury support the functional changes observed (Al-Saleem and the Clinical Committee on Mercury Poisoning 1976; Cinca et al.1979; Davis et al. 1974; Miyakawa et al. 1976). Limited information was located regarding exposure levels associated with the above effects, but **increased tremors and cognitive difficulties** are sensitive end points for chronic low-level exposure to metallic mercury vapor (Fawer et al. 1983; Ngim et al. 1992).

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Female dentists and dental assistants exposed to metallic mercury vapors had increased reproductive failures (spontaneous abortions, stillbirth, and congenital malformations) and irregular, painful, or hemorrhagic menstrual disorder (Sikorski et al. 1987). Correlations were observed between the incidence of these effects and hair mercury levels. Rowland et al. (1994) report that female dental assistants with high occupational exposure to mercury were found to be less fertile than controls. Rowland et al. (1994) found that 20% of the women in their final evaluation who prepared more than 30 amalgams a week had 4 or more poor mercury-hygiene factors.

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Inhibition of follicular maturation and normal uterine hypertrophy, morphological prolongation of the corpora lutea, and alteration of progesterone levels were observed. Collectively, these results suggest that at sufficiently high mercury concentrations, **men may experience some adverse effects on testicular function and women may experience increases in abortion, decreases in conceptions, or development of menstrual disorders. Developmental Effects. Mercury is considered to be a developmental toxicant. Metallic mercury vapor may be transferred across the placenta** (Greenwood et al. 1972).

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Removal of existing amalgams, if improperly performed or not indicated, may result in unnecessarily high exposure to mercury. Levels of mercury release for various dental procedures have been reported by Eley (1997). In 1990 in the United States, over 200 million restorative procedures were provided of which dental amalgam accounted for roughly 96 million (DHHS 1993). A survey conducted by the American Dental Association in 1991 demonstrated that nearly half of the 1,000 American adults surveyed believed that health problems could develop as a result of dental amalgam (ADA 1991). Increases in life expectancy and increases in the numbers of older adults who still have their permanent teeth will result in longer mercury exposure duration's from dental amalgam, which may result in new or increased severity of effects. Since these guidelines and regulations (including the MRL) are themselves extrapolated from the hazardous effects literature, there is some circularity in the argument that exposures of mercury form amalgam that exceed guidelines like the MRL (or other standard) "support" the position that mercury amalgams pose a health risk. This aspect of the controversy will only be satisfactorily resolved with better toxicity and pharmacokinetic data for chronic low-level mercury exposure from amalgams.

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Siblerud and Kienholz (1997) investigated whether mercury from silver dental fillings (amalgam) may be an etiological factor in multiple sclerosis (MS). **MS subjects with amalgams were found to have significantly lower levels of red blood cells, hemoglobin, and hematocrit compared to MS subjects with amalgam removal.** Hair mercury was significantly higher in the MS subjects compared to the non-MS control group (2.08 versus 1.32 ppm). A health questionnaire found that MS subjects with amalgams had significantly more (33.7%) exacerbation's during the past 12 months compared to the MS volunteers with amalgam removal: 31% of MS subjects felt their MS got better after amalgam removal, 7% felt it was eliminated, 33% felt no change, and 29% believed the condition got worse. In addition, 17% of the MS with amalgam group had more neuromuscular symptoms compared to the amalgam removal group. Bjorkman et al. (1997) examined the mercury concentrations in saliva, feces, urine, whole blood, and plasma before and after removal of dental amalgam filling in 10 human subjects. Before removal, the median mercury concentration in feces was more than 10 times higher than in samples taken from an amalgam-free reference group of 10 individuals. The authors concluded that while mercury amalgam fillings are a significant source of mercury in saliva and feces, those levels decrease considerably following amalgam removal. Further, the gastrointestinal uptake of mercury seen in conjunction with removal of amalgam fillings appears to be low.

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Hultman et al. (1994) studied the effects of dental amalgams in in-bred mice genetically susceptible to mercury-induced immunotoxic effects. In this study, not only did the dental amalgam implantation cause chronic stimulation of the immune system with induction of systemic autoimmunity, but the implantation of silver alloy not containing mercury also induced autoimmunity, suggesting that other metals have the potential to induce autoimmunity in that genetically susceptible strain of mice. Accumulation of heavy metals from dental amalgams, as well as from other sources, may lower the threshold of an individual metal to elicit immune aberrations, which could lead to over autoimmunity.

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Intake of elemental mercury from dental amalgams is another major contributing source to the total mercury body burden in humans in the general population (WHO 1990, 1991). Because the two major sources of mercury body burden include dietary intake and intake from dental amalgams, mercury is present at low concentrations in a variety of human tissues. Mercury has been detected in blood, urine, human milk, and hair in individuals in the general population. Dentists and dental staff, and individuals involved in disposal or recycling of mercury-contaminated wastes are also at risk of exposure. **Members of the general population with potentially high exposures include individuals with a large number of dental amalgams.**

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Dental Amalgams Recent animal and human studies have also identified the uptake, distribution, and rate of excretion of elemental mercury from dental amalgams as another significant contributing source to mercury body burden in humans (Bjorkman et al. 1997; Lorscheider et al. 1995). A summary of contributing sources of mercury to the human body burden is presented in Table 5-12. Because of the wide range of potential exposures and the high retention rate for elemental mercury, **dental amalgams potentially represent the largest single contributing source of mercury exposure in some individuals with large numbers (>8) of amalgam fillings.**

Dental amalgams may contain 43-54% elemental mercury (DHHS 1993). **A single amalgam filling with an average surface area of 0.4cm has been estimated to release as much as 15 hg mercury/day**, primarily through mechanical wear and evaporation, but also through dissolution into saliva (Lorscheider et al. 1995). The rate of release is influenced by chewing, bruxism (grinding of teeth) food consumption, tooth brushing, and the intake of hot beverages (Weiner and Nylander 1995). For the average individual with eight occlusal amalgam fillings, 120 Hg of mercury could be released daily into the mouth, and a portion of that swallowed or inhaled (Lorscheider et al. 1995). Experimental results regarding estimated daily dose of inhaled mercury vapor released from dental amalgam restorations are few and contradictory (Berglund

1990). More recently, Bjorkman et al. (1997). Various laboratories have estimated the average daily absorption of amalgam mercury ranging from 1 to 27 Hg, with levels for some individuals being as high as 100 hg/day (Bjorkman et al. 1997; Lorscheider et al. 1995; Weiner and Nylander 1995). Estimates of mean daily elemental mercury uptake from dental amalgams from these and earlier studies are summarized in Table 5-16. A report from the Committee to Coordinate Environmental Health and Related Programs (CCEHRP) of the Department of Health and Human Services determined that "measurement of mercury in blood among subjects with and without amalgam restorations… and subjects before and after amalgams were removed …provide the best estimates of daily intake from amalgam dental restorations. These values are in the range of 1-5 hg/day: 9DHHS 1993). Another source indicates that the consensus average estimate is 10 hg amalgam Hg/day (range, 3-17 hg/day) WHO 1991). However, Halbach (1994) examined the data from 14 independent studies and concluded that the probable mercury dose from amalgam is less than 10 hg/day. Most recently, Richardson (1995) computed a release rate per filled tooth surface as 0.73 hg/day-surface, with a standard deviation of 0.3 hg/day-surface and a "stimulation magnification factor" of 5.3, based on a weighted average enhancement of mercury vapor concentrations following chewing, eating, or tooth brushing reported in three amalgam studies.

By comparison to the estimated daily absorbance of mercury from dental amalgams (range, 3-17 hg), the estimated daily absorbance from all forms of mercury from fish and seafood is 2.31 hg and from other foods, air, and water is 0.3 hg (WHO 1991). These other sources taken together only total 2.61 hg/day, in comparison to estimates of 3-17 hg/day for dental amalgams. Assuming a person has a large numbers of amalgams, this source may account for 17 hg/day out of a total absorbance of 19.61 h/day, or 87% of the absorbed mercury. In contrast, in individuals with only a few amalgams, mercury from this source may account for only 3 hg mercury/day out of a total absorbance of 5.61 hg/day, or 53% of absorbed mercury, Halbach et. Al. (1994) concluded that the sum of the mercury uptake from dental amalgam and dietary uptake is still below the dose corresponding to the acceptable daily intake (ADI) of mercury. The ADI of 40 hg total mercury, 30 hg of which are allowed for methylmercury, results in a total dose of approximately 30 hg after accounting for absorption (Halbach 1994; WHO 1976). WHO (1990) estimates a daily absorption of 2.61 hg from background exposure for persons without amalgam exposure.

Urine

Urine is a common indicator used to assess occupational mercury exposure (EPA 1996d). Urinary mercury is thought to indicate most closely the mercury levels present in the kidneys (Clarkson et al. 1988b.) Several authors have related elevated urinary mercury levels to dental amalgams in individuals in the general population (Barregard et al. 1995; Skare 1995) and in dentist and dental personnel receiving occupational exposures (Akesson et al. 1991; Chien et al 1996; WHO 1991).