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THE IMPORTANCE OF MERCURY DETERMINATION AND SPECIATION TO THE HEALTH OF THE GENERAL POPULATION.

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ABSTRACT
It is well known that the toxicokinetics (i.e. absorption, distribution, metabolism and excretion) of mercury is highly dependent on the form of mercury to which a receptor has been exposed. The aim of this paper is to summarize the available health effects information for mercury and mercury compounds in the international scientific literature (1940-2003) and to point to the need for increased Hg control of water and food, including mercury speciation, especially in Mediterranean countries.

KEYWORDS: Mercury, toxicokinetics, health, speciation, Mediterranean countries.

INTRODUCTION
The toxicity of mercury is well-known for centuries. The first report pertaining to the toxicity of this metal and its compounds is probably in the works of Plenius Senior (23-79 A.D.) (Huber, 1997). During the Roman Empire, slavery at the Cinnabar mines was used as a terrible punishment for "disobedient" citizens. This was amounting to a slow, painful death (Pavlogeorgatos, 2001).
The first description of industrial poisoning from mercury use is found in 1557. The workers suffered from chronic exposure to inorganic mercury salt, which resulted in restlessness, depression, lack of concentration and the characteristic hand tremor (Pavlogeorgatos, 2001).
Centuries later in Lewis Caroll's "Alice in wonderland" the existence of mad hatters is mentioned (19 century A.C.), whose insanity was caused by the use of mercury nitrate solutions which were used to the cleaning of felt hats and the processing of beaver pelts which were in fashion at that time for hat-making (Shrader and Hobbins, 1983). This insanity was usually accompanied by a "curious gait", hand tremor, depression, tachycardia, concentration loss etc. The expression "mad as a hatter", was a result of the connection of this particular professional class to the neurological disturbance that is brought by inorganic mercury salt exposure.
In modern history, mass poisonings by mercury

compounds in many countries (US EPA, 1997b; Forstner - Wittmann, 1983), as for example in Japan on 1950, 1964, 1973 in Iraq on 1972 and in Canada in 1978, lead the scientific community to the intensification of research of the toxic effect of mercury to the living and non-living environment. Despite the fact that mercury is one of the most toxic metals with serious effects on humans and on the environment, its research was seriously delayed, compared to other metals. This could be explained by the following:

Mercury's ability to exist in several physical states and chemical forms at commonly - encountered conditions of temperature and pressure, and its propensity to undergo biological transformations, means that it is subject to complex and difficult-to-predict changes in concentration and form. Environmental monitoring studies thus must consider a variety of physical changes, geochemical reactions, and biochemical interactions in an attempt to understand the specific local conditions that contribute to mercury levels found in different environmental media and living things.

Mercury is a List I (EEC, 1976) substance and its presence in effluents is controlled by two EEC Directives (EEC, 1982; EEC, 1984).

All scientists who have studied mercury's behaviour, during the last decade, have faced the following problems (Pavlogeorgatos, 2001):

- Mercury has high detection limits in the most widely used analytical techniques used for the determination of heavy metals (AAS, ICP-AES).
- Serious contamination problems come up during the sampling, the pre-treatment and the analysis of samples.
- There is a lack of mercury concentrations in some of the existing reference materials.

So, the purposes of this paper are:

1. The survey of the scientific literature (from 1940 to 2003) relating to the effects of different mercury species on the human health.
2. To show the inadequacy of the current European legislation to protect the human health, as much as the environment, from mercury.
3. To indicate the need for increased mercury-detection controls in water and in food especially in the Mediterranean countries. The inhabitants of these countries belong to a high-risk population for exposure to mercury.

SOURCES OF MERCURY IN THE ENVIRONMENT

The main sources of mercury in the environment are presented in Table 1.

High-risk groups for mercury exposure

High-risk groups according to their mercury exposure are mainly:

1. **Industrial workers** (Limbong *et al.*, 2003; Vahter *et al.*, 2002; US EPA, 1997; Piikivini and Hanninen, 1989; Piikivini and Tolonen, 1989; Miller *et al.*, 1975; Barregard *et al.*, 1992; Langolf *et al.*, 1978; Forzi *et al.*, 1978)
2. **People living near point sources of mercury emissions** (Pavlogeorgatos, 2001; US EPA, 1997).
3. **People who consume large amounts of fish** (Watanabe *et al.*, 2003; Jewett *et al.*, 2003; Lopez - Alonso *et al.*, 2003; Tsuji and Robinson, 2002; Vahter *et al.*, 2002; Davis *et al.*, 2002; Santos *et al.*, 2002; Sanna *et al.*, 2002; De Santos *et al.*, 2000; Mergler, 2002; Boischio and Henshel, 2000; Airey, 1983).
4. **Dental professionals** (Sanna *et al.*, 2002; Hol *et al.*, 2001; US EPA, 1997).
5. **Chemists and chemical laboratories stuff** (Pavlogeorgatos, 2001; Dewhurst, 1974).

In Figure 1 is shown the geographical distribution of Mediterranean mines, which produce the largest quantities of mercury in the world. This fact, together with the fact that Mediterranean inhabitants belong to high-risk groups for mercury exposure 2 and 3, leads to the conclusion that South Europeans are among the most highly exposed to mercury compounds.

Toxicokinetics of mercury in humans

Mercury toxicity is caused, mainly, by the fact that it enters the living organism, and reacts with different enzymes inhibiting the catalysis of basic metabolic reactions (WHO, 1990; Public Health Statement, 1990; WHO, 1989; Kouimtzis, 1994).

The general population may be exposed to mercury compounds through inhalation of ambient air; consumption of contaminated food, water or soil; and/or dermal exposure to substances containing mercury. In addition, some quantity of mercury is released from dental amalgam.

It is well known that the toxicokinetics (i.e. absorption, distribution, metabolism and excretion) of mercury are highly dependent on the form of mercury to which a receptor has been exposed

Table 1. Sources of mercury in the environment
(Lopez Alonso *et al.*, 2003; Freed *et al.*, 2002; Sanna *et al.*, 2002; Ansari *et al.*, 1999; US EPA, 1997a and b; Obenauf and Skavroneck, 1997; Huber, 1997; Namasivayam and Periasamy, 1993; Jasinski, 1994; US EPA, 1992b; Lester, 1987; Nurnberg, 1985; WHO, 1989).

Surface sources of mercury		
Burning of oil and its products	Burning of coal	Sanitary landfill
Burning of the wastes and sludges	Burning of wood	Geothermic energy
Burning of rural by-products	The use of products made by peat	The use of paintings
Point sources of mercury		
Catalyst in the production of alkaline products	Amagalms (Dental work)	Sensors
Manufacturing and using of explosives	Used in batteries	Oscillators
Manufacturing and use of the fireworks	Cleaning solutions	Used in chemical laboratories
Use of some preservatives	Relays	Destroyed light bulbs
Used for cosmetics, medicines, and insecticides	Signal transmitters	Coverings of different paper forms
Medicines for poultry and farm animals	Rectifiers	
Industrial sources of mercury		
Sodium carbonate and chloride production units	Cinnabar (HgS) production units	Pulp and paper production units
Photographic equipment and consumables production units	Gold or silver mining and processing units	Electric and electronic appliance production units
Lead, copper and zinc mining and processing units	Plant chemicals production units	Cement production units
Units of secondary mercury production	Coal side products	Coal production units
Instrument production units	Fluorescent bulb recycling plants	Color paint production units
Light bulb production units	Furnaces	Battery production units
Explosives production units	Refineries	

Figure 1. Geographical distribution of mercury mines in the Mediterranean. (UNEP, 1987)
(● Highly productive mines, ❍ increased concentrations of mercury, ▲ formerly productive mines).

Table 2. Absorption and adsorption of different forms of mercury by the human body

Mercury form	Ways of absorption by the human organism	References
Elemental Hg	The respiratory absorption of elemental mercury is the major way of absorption in humans (>75-85% of the total uptake). Through the lungs it is eventually transported to the bloodstream. Gastrointestinal tract absorption is negligible (0.01%).	Loredo *et al.*, 2003; DeRouen *et al.*, 2002; Finkelman *et al.*, 2002; Nielsen - Kudsk, 1965; Oikawa *et al.*, 1982; Teisinger and Fiserova-Bergova, 1965; Hursh, 1985; Hursh *et al.*, 1985; Levine *et al.*, 1982; Berlin *et al.*, 1969; Bornmann *et al.*, 1970; Berlin, 1986; US EPA, 1997c.
Inorganic Hg compounds	The degree of absorption of inorganic mercury by the gastrointestinal tract varies, and depends on which mercuric salt is involved in this process (7-15%). Absorption diminishes with the decrease in solubility. Estimates on the degree of uptake of inorganic mercury vary, though it is greater than 20% of the total Hg uptake. In general, bivalent Hg, because it has a greater solubility than the univalent, is more absorbed and more toxic. There is no data about dermal absorption.	Loredo *et al.*, 2003; Clarkson, 1989; Miettinen, 1973; Rahola *et al.*, 1973; Foulkes and Bergman, 1993; US EPA, 1997c; Endo *et al.*, 1990; Sin *et al.*, 1983.
Alkyl mercury compounds	Methyl-mercury is rapidly and in a large degree absorbable (95%) by the gastrointestinal system. Information pertaining to the inspiratory absorption of this compound is limited. The percentage of dermal absorption is unknown (3-5% in laboratory animals).	Loredo *et al.*, 2003; Iyengar and Rapp, 2001; Fang, 1980; US EPA, 1997c; Dunn *et al.*, 1981; Aberg *et al.*, 1969; Miettinen, 1973; Kershaw *et al.*, 1980; Miettinen *et al.*, 1971; Sherlock *et al.*, 1982; Skog and Wahlberg, 1964.
Other organic Hg compounds.	There is a small amount of absorption by the respiratory and dermal system, and complete absorption by the gastrointestinal system (this is true for acetic phenyl-mercury and less so for methoxy-ethyl-mercury).	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.

(US EPA, 1997). As a result we must approach differently the toxicokinetics of each form of mercury in the human organism according to:

- Absorption (Table 2)
- Excretion (Table 3)
- Distribution (Table 4)
- Biological action (Table 5)
- Affected organs (Table 6)
- Detoxification and suppression (Table 7), and
- Borderline concentrations of different Hg forms in the human body (Table 8).

On Table 9 the latest data on hazard identification and dose-response assessment are summarized, according to the U.S. EPA.

Finally on Table 10 the effects of mercury compounds on human health are summarized according to the international scientific literature (from 1940 to 2003).

Table 3. Excretion of different forms of mercury by the human body

Form of mercury	Ways of excretion from the human body	References
Elemental Hg	Elemental Hg is excreted from the human body in the urine, feces, expired air, sweat and saliva. Variations of the form of excretion depend on the degree of oxidation of elemental Hg to mercuric mercury. In general, a low-level exposure is related to a, mainly, fecal excretion, while a high-level exposure is related to a mainly urinary.	Roels *et al.*, 1991; Stopford *et al.*, 1978; Hursh *et al.*, 1976; Cherian *et al.*, 1978; Magos, 1973; Roels *et al.*, 1987; Roels *et al.*, 1985; Lovejoy *et al.*, 1974; Rothstein and Hayes, 1964; US EPA, 1997c; Stratis and Zachariades, 1989.
Inorganic Hg compounds	On a low-level exposure, it is excreted mainly by the stool (approximately 85%), while on a high-level exposure mainly by the urine (approximately 35%).	Miettinen, 1973; Rahola *et al.*, 1973; Rothstein and Hayes, 1964; Berlin, 1986; Cherian *et al.*, 1978; Ballatori and Clarkson, 1982; Yoshida *et al.*, 1992; US EPA, 1997c; Stratis and Zachariades, 1989.
Alkyl Hg.	Its clearance from the human organism is accomplished by excretion in stool, maternal milk and urine.	Myers G.J. *et al.*, 2000; Vahter *et al.*, 2000; Drexler and Schaller, 1998; Aberg *et al.*, 1969; Bernard and Purdue, 1984; Miettinen, 1973; Smith *et al.*, 1970; Norseth and Clarkson, 1971; Clarkson, 1993; Rowland *et al.*, 1980; Stratis and Zachariades, 1989; Farris *et al.*, 1993; Hollins *et al.*, 1975; Thomas *et al.*, 1987; Bakir *et al.*, 1973; Sundberg and Oskarson, 1992; Greenwood *et al.*, 1978; Skerfving, 1988.
Other organic Hg compounds.	It is the same as the inorganic mercury.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.

CONCLUSIONS

As Tables 1-10 indicate the main conclusions of this report are:

1. Mercury causes serious damages to the human organism, mainly of a neurological nature, which can even lead to the death of the exposed individual. The severity of these damages depends on the quantity acquired, the duration of the exposure and the chemical species of mercury.
2. The inhabitants of the Mediterranean basin belong to the high-risk groups for exposure to different forms of mercury, because of their dietary habits and their proximity to natural mercury sources.
3. The current European legislation sets the maximum allowed limits for total mercury concentration in drinkable water and in food (mainly of sea origin), but does not demand the chemical speciation of the detected mercury. Also, it should be mentioned, that in many Mediterranean countries the food and water control for mercury detection is negligent and occasional, because mercury detection demands additional equipment, specialized staff and meticulous care in sampling and analysis.

Table 4. Allocation of different forms of mercury in the human body

Forms of mercury	Allocation in the human organism	References
Elemental Hg	It is mainly transported by red blood cells (>98% of the total uptake) and accumulates mainly on the cerebral gray matter (especially the fetal during pregnancy).	US EPA, 1997c; Hursh *et al.*, 1988; Hursh *et al.*, 1985; Hursh *et al.*, 1976; Nordberg and Serenius, 1969; Rothstein and Hayes, 1964; Takahata *et al.*, 1970.
Inorganic Hg compounds	It is allocated by bloodstream to the whole human organism and accumulates mainly in liver and kidneys.	Vahter *et al.*, 2002; Hac *et al.*, 2000; Newton and Fry, 1978; Rothstein and Hayes, 1960; Cember, 1962; Piotrowski *et al.*, 1975; US EPA, 1997c; Piotrowski *et al.*, 1973; Stratis and Zachariades, 1989.
Alkyl Hg	Circulates unchanged in the bloodstream for long periods of time. A percentage of the total (about 10%) accumulates in the brain and the placenta of pregnant women. Also in spleen, heart and hair.	Ehrenstein *et al.*, 2002; Vahter *et al.*, 2002; Hac *et al.*, 2000; Iyengar and Rapp, 2001; Clarkson, 1972; Hansen, 1988; Hansen *et al.*, 1989; Nielsen *et al.*, 1994; Soria *et al.*, 1992; Suzuki *et al.*, 1984; US EPA, 1997c.
Other organic Hg	Because of their dissociation to bivalent Hg in the liver, it is the same as the inorganic mercury.	US EPA, 1997c; Pavlogeorgatos, 2001.

Table 5. Biological action of different forms of mercury in the human body

Forms of mercury	Biological action	References
Elemental Hg	It easily enters tissue and red blood cells where is oxidized to bivalent mercury, with the help of a catalase.	Halbach and Clarkson, 1978; US EPA, 1997c; Stratis and Zachariades, 1989.
Inorganic Hg compounds	Because of its increased chemical relation to the SH- groups, found on protein molecules, it inhibits enzyme action. It has an effect on the metabolism of amino acids in the brain and blocks the functions of cell membrane, because of its chemical relation to the PO^4 -groups. But, there are also reports of a reduction of inorganic mercury compounds to the elemental form of this metal.	Dunn *et al.*, 1981; Clarkson and Rohstein, 1964; Sugata and Clarkson, 1979; US EPA, 1997c.
Alkyl Hg	Using red blood cells it penetrates the blood-brain barrier, and inhibits the enzyme action of glycolysis and the protein synthesis mechanisms.	Ehrenstein *et al.*, 2002; US EPA, 1997c; Pavlogeorgatos, 2001
Other organic Hg compounds	It dissociates in the liver to produce bivalent and benzol. Accordingly, it has the same action as inorganic mercury.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.

Table 6. Critical organs of the human body in its exposure to different forms of mercury.

Form of mercury	Critical organs	References
Elemental Hg	In a brief, high-level exposure, the lungs. In a long-term exposure the Central Nervous System (CNS) and especially the brain.	Karimi *et al.*, 2002; Adams *et al.*, 1983; Founds *et al.*, 1987; McFarland and Reigel, 1978; Snodgrass *et al.*, 1981; Sexton *et al.*, 1978; Vroom and Greer, 1972; US EPA, 1997c; Stratis and Zachariades, 1989.
Inorganic Hg compounds	Mainly the kidneys.	Vahter *et al.*, 2002; Carrier *et al.*, 2001 (a and b); US EPA, 1997c; Pavlogeorgatos, 2001; Stratis and Zachariades, 1989.
Alkyl Hg	Brain and CNS.	Ehrenstein *et al.*, 2002; Iyengar and Rapp, 2001; US EPA, 1997c; Pavlogeorgatos, 2001; Stratis and Zachariades, 1989.
Other organic Hg compounds	In case of a chronic exposure the kidneys and probably the liver.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.

Table 7. Detoxification and action suppression of different forms of mercury in the human body.

Mercury form	Detoxifying compounds	References
Elemental Hg	Vitamin E is reported to be a protective agent. Additionally, ethanol reduces the human organism ability for absorption of elemental mercury, possibly by suppressing the activity of the catalase, which oxidizes it to produce bivalent Hg. Tellurium also appears to have a protective role.	Dunn *et al.*, 1981; Nielsen - Kudsk, 1965; US EPA, 1997c; Stratis and Zachariades, 1989; Magos and Webb, 1979; Khayat and Dencker, 1982, 1984a and b.
Inorganic Hg compounds	Metaltheionin has a protective role. Also various mercury-chelating compounds (e.g. bimercapto-propanol), accelerate its excretion. Finally, it is worth mentioning that selenium seems to have a protective action by binding Hg to HgSe and limiting its acute action on intestine and kidneys. Tellurium also has a protective role.	Hol *et al.*, 2001; Magos and Webb, 1979; US EPA, 1997c; Khayat and Dencker, 1984a; Zalups and Cherian, 1992; Stratis and Zachariades, 1989.
Alkyl Hg	Evidence from other mammals indicates that selenium has a protective role against organic mercury also. It is reported, without impressive clinical results, that the N-acetyl product of D, L penicilamine accelerates its excretion. Also vitamin E reduces the toxicity and increases survival chances after an exposure to methyl-mercury.	Hol *et al.*, 2001; Myers *et al.*, 2000; Grandjean, 1992; Ballatori and Clarkson, 1982; Welsh, 1979; US EPA, 1997c.
Other organic Hg compounds	Glutathion probably catalyzes the rapid dissociation of the Hg-C bond.	US EPA, 1997c; Fukino *et al.*, 1992; Girardi and Elias, 1991.

Table 8. Borderline concentrations of different forms of mercury in the human body

Mercury form	**Borderline concentration**	**References**
Elemental Hg	No symptoms reported on <10 μg Hg m^{-3} of air. Symptoms of micro-mercurism on 10-50 μg Hg m^{-3} of air. Symptoms of mercurism on 60-100 μg Hg m^{-3} of air. Symptoms of the CNS 100-270 μg Hg m^{-3} of air. A concentration of 10-70 μg g^{-1} (w/w) in the kidneys causes proteinuria. Concentrations of 70-140 μg l^{-1} in the bloodstream or 300-600 μg l^{-1} in the urine cause tremor.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001; Roels *et al.*, 1982; Verbeck *et al.*, 1986.
Inorganic Hg compounds	Micro-mercurism from 10-50 μg Hg m^{-3} of air. Chronic mercurism >100 μg Hg m^{-3} of air. Concentrations from 10-40 μg Hg g^{-1} of renal tissue cause temporary damage, while in >100 μg Hg g^{-1} causes serious kidney damage	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.
Alkyl Hg	1.2-3.4 μg MeHg l^{-1} in the brain cause the first symptoms. Concentrations of 6-17 μg MeHg l^{-1} in brain are fatal. Lethal doses for liver respectively are >10 μg MeHg g^{-1} and for blood >3000 ng MeHg g^{-1}. In general, on levels higher than 25mg/70kg of body weight sense disturbances are caused, over 90 mg dysarthria and over 170 mg deafness.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.
Other organic Hg compounds	A concentration of 6 mg l^{-1} in the urine causes the appearance of albuminuria. Ingestion of a quantity <1250 mg of salt causes very mild gastrointestinal disturbances. On levels of between 0.2 and 5.1 mg m^{-3} of atmospheric air no symptoms were reported.	US EPA, 1997c; Stratis and Zachariades, 1989; Pavlogeorgatos, 2001.

Table 9. Summary of U.S. EPA Hazard Identification /Dose-response Assessment for mercury and Mercury compounds (US EPA, 1997c).

Form of mercury Parameter	**Elemental Hg**	**Inorganic Hg**	**Organic Hg**
Oral RfD [A] (mg kg^{-1}-day)	n/a [A]	0.0003 (mercuric chloride) [B]	0.0001 (MeHg) [E]
Inhalation RfC (mg m^{-3})	0.0003 [B]	Not verifiable[D]	n/a
Cancer Weight -of - evidence Rating	D, not classifiable as to human carcinogenicity [F]	C, possible human carcinogen [F]	C, possible human carcinogen [F]
Cancer Slope Factor	n/a	n/a	n/a
Germ Cell Mutagenicity	Low weight of evidence	Moderate weight of evidence	High weight of evidence
Developmental Toxicity Data Base Characterization	Insufficient human evidence; sufficient animal evidence	Insufficient evidence	Sufficient human and animal data

A: Not available; data do not support development of a value at this time.
B: Critical effect is neurological toxicity (hand tremor; increases in memory disturbances; slight subjective and objective evidence of autoimmune dysfunction) in adults.
C: Critical effects is renal toxicity resulting from an autoimmune disease caused by the accumulation of a hapten - mercury complex in the glomerular region of the kidneys.
D: Data were judged insufficient for calculation of RfC.
E: Critical effect is neurological toxicity in progeny of exposed women, RfD calculated using a benchmark dose (10%).
F: US EPA categorizes all chemical compounds into five categories according to their connection to carcinogenesis. Ranging from A (proven carcinogenic compounds) to E (proven non-carcinogenic compounds).

Table 10. Effects of mercury compounds on human health.

Effect	**References which support it**
Aneuploidy	Renzoni *et al.*, 1998; Verschaeve *et al.*, 1976.
Autoimmune diseases (S.L.E., Scleroderma, Glomerulonephritis)	Hess, 2002; Lawrence and MacCabe, 2002; Sondreal *et al.*, 2002.
Birth of a dead fetus	Vahter *et al.*, 2002; Sikorski *et al.*, 1987
Blindness - Visual disturbances	Finkelman *et al.*, 2002; Mergler, 2002; Altmann *et al.*, 1998; Snyder and Seelinger, 1976; Amin - Zaki *et al.*, 1974.
Characteristic hand tremor	DeRouen *et al.*, 2002; Harada *et al.*, 2001; Drasch *et al.*, 2001;Harada *et al.*, 1999; Kang-Yum and Oransky, 1992; Roels *et al.*, 1982; Verbeck *et al.*,1986; Harada, 1978; Derobert and Tara, 1950.
Chromosomal abnormalities	Santos *et al.*, 2002; Renzoni *et al.*, 1998; Popescu *et al.*, 1979.
Coma	Cinca *et al.*, 1979.
Congenital malformations	Vahter *et al.*, 2002; Myers *et al.*, 2000; Sikorski *et al.*, 1987.
Death	Mergler, 2002; Myers *et al.*, 2000; Mitsumori *et al.*, 1990; Tamashiro *et al.*, 1984; Bakir *et al.*, 1973; Mitsumori *et al.*, 1981; Troen *et al.*, 1951.
Delay in speech and in walking and mental retardation of new-borns	Vahter *et al.*, 2002; Mergler, 2002; Redwood *et al.*, 2001; Myers *et al.*, 2000; Futatsuka *et al.*, 2000; Sondreal *et al.*, 2000; Marsh *et al.*, 1987; Harada, 1978.
Depression	Mergler, 2002; DeRouen *et al.*, 2002; US EPA, 1997c.
Difficulty in speech	DeRouen *et al.*, 2002; Futatsuka *et al.*, 2000; Bakir *et al.*, 1980; Cinca *et al.*, 1979; Harada, 1978; Bakir *et al.*, 1973.
Dyspnoia-Pneumonitis	DeRouen *et al.*, 2002; Bluhm *et al.*, 1992; Snodgrass *et al.*, 1981; Hallee, 1969.
Fetal miscarriage	Karimi *et al.*, 2002; Cordier *et al.*, 1991; Afonso and DeAlvarez, 1960.
Growth retardation in exposed children	Akagi *et al.*, 2000.
Hallucinations	Marsh *et al.*, 1987; Bakir *et al.*, 1980; Bakir *et al.*, 1973; Harada, 1978.
Hypertension, tachycardia	Soni *et al.*, 1992; Fagala and Wigg, 1992; Snodgrass *et al.*, 1981; Hook *et al.*, 1954.
Immune system suppression	Mattingly *et al.*, 2001; Sondreal *et al.*, 2000

Effect	**References which support it**
Increased incidence of leukemia (in methyl-mercury exposure)[1]	Santos *et al.*, 2002; Janicki *et al.*, 1987.
Increased incidence of liver cancer (in methyl-mercury exposure)[1]	Tamashiro *et al.*, 1986.
Insanity	Davis *et al.*, 1974.
Lack of cooperation abilities.	Derobert and Tara, 1950.
Loss of concentration	Mergler, 2002; DeRouen *et al.*, 2002; Redwood *et al.*, 2001; Clarkson *et al.*, 1976; Nordberg and Strangert, 1976; WHO, 1976.
Loss of hearing	Mergler 2002; Harada *et al.*, 2001; Amin-Zaki *et al.*, 1974.
Loss of memory	DeRouen *et al.*, 2002; Redwood *et al.*, 2001; Drasch *et al.*, 2001; US EPA, 1997c.
Loss of the touch sensation	Harada *et al.*, 2001; Mergler, 2002; Harada *et al.*, 1999; Hook *et al.*, 1954.
Lung cancer	Amandus and Costello, 1991; Barregard *et al.*, 1990; Buiatti *et al.*, 1985; Ellingsen *et al.*, 1992.
Male subfertility	Dickman and Leung, 1998.
Minamata syndrome: motor disturbance, seizures, retardation, palsy in the developing fetus	Sondreal *et al.*, 2000.
Muscular weakness	Harada *et al.*, 2001; Kang-Yum and Oransky, 1992; McKeown-Eyssen *et al.*, 1983
Nausea, vomiting up to severe gastroenteritis	Harada *et al.*, 2001; Afonso and DeAlvarez, 1960; Troen *et al.*, 1951.
Paralysis	Harada *et al.*, 2001; US EPA, 1997c.
Pneumonia	Hallee, 1969.
Restlessness	US EPA, 1997c.
Up to 55% reduction on human brain weight and volume	Clarkson *et al.*, 1976; Nordberg and Strangert, 1976; WHO, 1976.
Walking deficits - Ataxia	Futatsuka *et al.*, 2000; Myers *et al.*, 2000; Cinca *et al.*, 1979; Von Burg and Rustam, 1974 a and b; Hunter *et al.*, 1940.

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