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Dear Madam, Dear Sir,

Please find herewith the final report on the mercury amalgams and a booklet which summarizes the main information.

The report of the working group on the mercury amalgams, set up at Afssaps in August 2003, brings up to date the knowledge on this subject gathered since 1998. It explains also the setting up of a multi-field network of evaluation and gives recommendations to health professionals as well as to the public.

It will be available on the agency website [www.afssaps.sante.fr](http://www.afssaps.sante.fr) at the end of November ; a press release will be distributed on this occasion.

Best regards.



Jean Marimbert

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- Report on the mercury amalgams
- Booklet on the mercury amalgams
- List of the multidisciplinary network referents
- Summary on the results of the Afssaps working group on dental amalgams

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## Mercury amalgam report summary

Use of mercury amalgams for dental care still remains authorized worldwide. In fact, no country banned them although four member states in UE (Austria, Denmark, Germany and Sweden) have set some limitations.

Safety of dental amalgams has been already assessed in France by the Council of Public Health (CSHPF) in 1998. The ensuing report stated that mercury exposure level from dental amalgams was too low to induce any dose-dependent deleterious effect and concluded that no systemic toxic effect due to mercury released from amalgams had been reported in the scientific literature.

In 2003, Afssaps has set up a working group to update this report on three topics: odontological practice, biometry and clinical effects. The experts of the scientific panel have thoroughly analyzed 269 articles published in peer-reviewed scientific journals from 1997 to 2005 and adopted a consensus report on the safety of dental amalgams.

### **Basic information on the amalgams**

Mercury reacts at ambient temperature with a mixture of powdered metals to produce a crystallized solid alloy named amalgam. Within the alloy, mercury is present as stable silver or tin compounds. However, some elemental mercury may be released during condensation, polishing or removal of the dental amalgams. Mercury vapour is also present in air inside the oral cavity in amounts directly related to the number of restorations. In addition, some particles of amalgams may be mechanically released by chewing and subsequently drained by saliva into the gastrointestinal tract.

### **Chemical species and kinetics of mercury in the body**

Mercury may enter the body as three chemical species: elemental mercury (amalgams), inorganic mercury (mercuric salts) and organic mercury mainly originating from food (methylmercury). Uptake of ingested inorganic species of mercury in the gastrointestinal tract is low (< 1 % for elemental mercury metal and 5 to 10 % for mercuric salts). A small fraction (~ 10 %) of mercury vapour released in mouth air may be absorbed partly in the lungs. Contrastingly, intestinal absorption organic mercury present in food as methylmercury is nearly complete (~ 90 %).

Several calculation methods have been proposed to evaluate the amount of mercury released by the amalgams and stored in the organism. Consensual values 3 to 4 µg/day appear sound and realistic. Such amounts lie far below those likely to elicit sub-noxious effects.

### **Determination of mercury in biological media**

Total mercury in blood mainly reflects organic mercury originating from food and is a very poor marker of mercury released by dental amalgams. Reference values for the general population within the EU are less than 10 µg/l.

A positive correlation has been observed between mercury in blood plasma and the number of amalgams. Plasmatic inorganic mercury is raised by 0,1 nmol/l (0,02 µg/l) per surface of amalgam, with large individual variations. Reference values for the general population are less than 4 µg/l.

The relation between urinary mercury excretion and the numbers of dental amalgams is well established. However other factors influence urinary mercury in particular the seafood consumption and smoking habit.

Urinary mercury in subjects with amalgams is clearly higher than in those without amalgams but remains substantially lower than the threshold for toxic effects (50 µg/g creatinin) or for biological response (30 µg/g creatinin). Reference values for the general population are less than 7 µg/l, that is, 5 µg/g creatinin.

Many studies have been conducted to evaluate the benefits of mercury chelation to better characterize an excessive body burden. Most popular chelating agents are DMPS - not approved in France - and DMSA, both administered orally. It is well established that increase in urinary excretion of mercury after administration of a chelating agents is higher in the subjects with amalgams than in those without amalgam. However, among amalgam bearers, excretion levels are not significantly higher in subjects exhibiting symptoms claimed to be linked to amalgams, than in non symptomatic subjects. Chelator-stimulated mercury excretion test appears clearly inappropriate to characterize a mercury overload in "sensitive" subjects.

In saliva, mercury levels are subject to large variations and strongly depend upon the sampling protocol. Scientists of the panel are not aware of the existence of a standardized protocol for sampling and analyzing mercury in saliva. As can be expected, salivary mercury is higher in subjects with amalgams, but the marked differences in bioavailability between mercury species render total mercury determination in this fluid unpredictable of both the amount of absorbed mercury and body burden.

Hair is recognized as a tissue accumulating organic mercury, primarily of food origin (methylmercury). Hence, scalp-hair mercury is not a good descriptor of mercury accumulation due to dental amalgams.

The mercury content of stools basically reflects the unabsorbed fraction of ingested mercury released by the amalgams. In addition, the heterogeneity of stools, analytical pitfalls and absence of reliable reference values, make this marker inappropriate for evaluating either mercury intake or body burden.

### **Clinical aspects: causality link analysis**

The oral lichen planus (OLP) can be related to sensitization with the mercury of the amalgam fillings but removal of the amalgam filling in OLP patients should only be considered when the amalgam is adjacent to mucosal lesion.

Epidemiological surveys and lymphocytic reaction studies, failed to demonstrate any nephrotoxic effect related to mercury released by the dental amalgams.

The expert panel scientist consider that several recent studies have clearly demonstrated that the various symptoms reported by "sensitive" subjects are not due to mercury released by dental amalgams. Studies with conventional markers of mercury exposure, and more particularly urinary mercury, do not show a greater accumulation of mercury in symptomatic subjects.

The suspicion of a causality link between mercury released by dental amalgams, decline of cognitive performances and the onset of dementia, more particularly Alzheimer's disease, was not confirmed.

Several epidemiologic studies, some with a limited number of participants, don't show any association between the presence of amalgams and multiple sclerosis. However, two of them are close to the statistical significativity. These results must be interpreted with caution considering the implication many other genetic, geographical or environmental factors.

### **Multidisciplinary survey protocol**

Within the framework of the medical device alert system, the French Health Products Safety Agency (Afssaps) has received a hundred of declarations stating "presumptions of intoxication caused by heavy metals" liable to point to the use of mercury in dental fillings. Most of these declarations recalled a model letter pointing the articles of the Public Health Regulations and the legal obligations of Afssaps ; nevertheless, as these letters offered no description, however cursory, of the plaintiffs'



pathologies, they could not be investigated by Afssaps. However, eight declarations contained information liable to be examined. In all these cases, the responsibility of mercury fillings for such pathologies going from sleep disorders to immuno-defective or neuro-degenerative illnesses had to be discarded.

In the future, in order to be able to exploit received information in a rigorous and standardized way, the working group has established a protocol for collecting clinical and analytical data. A network of referents has been set up all over the country ; the referents are odontologists in hospital and doctors from the 13 Poison Centres or Toxicovigilance Centres, or the Pharmacovigilance Centres in those areas where there are no PC or TVC. This protocol does not substitute for the legal obligations dental surgeons have to report, within the framework of the medical device alert system, any incident or risk of serious incident when working with a medical product, to Afssaps. An assessment of the data collected by Afssaps according to this protocol will be made in one year time with an information feedback towards the referents.

Rapport

# Le mercure des amalgames dentaires

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Agence française  
de sécurité sanitaire  
des produits de santé

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