We are encouraged by the FDA's recent reopening of the comment period for the proposed 2002 rule regarding the classification of dental amalgam mercury. We also appreciated the recent opportunity to meet with both Associate Commissioner of Science Dr Norris Alderson as well as the Dental Branch, in order to provide FDA with the scientific basis for our 2007 position statement (see appended below: SAB-Position Paper 2007) on dental amalgam. Included in the peer-reviewed scientific papers we provided to Dr Alderson and the Dental Branch were a sampling of some of the more important studies published subsequent to the September 6&7, 2006 Joint committee of FDA Advisors. At that meeting a majority vote the Joint Committee concluded that FDA's draft White Paper had significant limitations - including a failure to identify significant gaps in the scientific knowledge (particularly with respect to exposure levels) , and a lack of attention to sensitive subpopulations. Because of those significant limitations, the majority of the Joint Advisory Committee voted that the conclusion of the draft White Paper (that amalgam was 'safe') was not "reasonable". The purpose of this submission is to address some of these limitations. We are of the opinion that the evolving science increasingly reinforces our position that **the continued use of dental amalgam mercury creates unacceptable risks to all members of the public, but especially to children and women of childbearing age.** For example, the obvious retention of mercury from dental amalgams, as determined by low urinary mercury excretion by boys versus girls, indicates that the safety of mercury exposure to males with increasing testosterone levels may be a significant problem that has been overlooked and that this population may be at an even greater risk.

1) Mercury Exposure Levels from Dental Amalgam and Resulting Human Body Burden

Aposhian (attachment: Aposhian, 1992) documented the fact , now universally accepted by the scientific community, that dental amalgam fillings contribute the majority of mercury body burden in the general population. These findings have been corroborated by other research including human cadaver studies. Further, it is well known that when mercury from amalgam passes to the cord blood, it will reach the fetus and accumulate there. Haley (attachment: Medical Veritas AD) quantitatively measured mercury release from dental amalgams ranging from 4 - 22 micrograms/cm2 per day - "without galvanism, excess heat or pressure from chewing - all factors that increase mercury release from amalgams in the mouth". This study was done using very small single-spill fillings in a sealed container. These measurements showed that mercury release from amalgams vastly exceed the ‘estimated’ release reported by ADA 'authority' Rodney Mackert, DDS, who claimed that 7 fillings release only a single microgram of mercury per day - according to a Wall Street Journal article. It is important to note that Mackert, rather than directly measuring the actual quantity of mercury released by amalgams, instead "estimated" the amount of mercury released from amalgam fillings by looking at the mercury level in the urine of several test subjects. Mackert has no training in toxicology as he is a practicing dental materials expert. It is well established that less than 10% of mercury leaves the body by the kidney/urinary

route (the vast majority leaving by the bilary transport/fecal route). As a result of this flawed methodology the ADA estimated level of mercury release by amalgam grossly understates the amount of the mercury released. A study done by Dr. David Quig of Doctor's Data showed that an average of 60 micrograms are excreted daily in the feces of the average amalgam bearer. Therefore, if only 1 microgram were excreted by the required 7 amalgams, as suggested by Mackert and the ADA, to reach this average fecal excretion rate a person would have to have 420 amalgams.

2) Sensitive Subpopulations

Mercury exposure can no longer escape public knowledge since the appearance of the urinary prophyrin profile as a clinical test for showing toxic effects of mercury on humans. This test is readily available to physicians and dentists that are concerned with the possibility of mercury toxicity contributing to the illnesses of their patients and it will highlight the mercury exposures received from existing dental amalgams. Using this methodology Woods (attachment: Woods 2005 abstract) demonstrated that 85% of dentists with low-level occupational mercury exposure had aberrant urinary prophyrin profiles (i.e. mercury negatively affected those enzymes required for the synthesis of heme a major natural compound needed for oxygen transport by red cells and for activity of the P-450 enzymes that detoxify the body) due to this mercury exposure, and that 15% of these affected dentists and dental technicians exhibited a genetic polymorphism in the CPOX gene showing an even more deleterious effect on their porphyrin profile and subsequent heme synthesis. This altered porphyrinogenic response might serve as a biomarker of both mercury exposure and susceptibility to mercury toxicity.

Woods (attachment: IMT-Woods, 2007) measured urinary mercury levels in the Portuguese subjects in the NIH children's amalgam trials (CAT study). The data clearly showed that boys excrete less mercury via the urinary pathway than girls and thus have a larger mercury body burden than girls. Figure 3 in this study (attachment: Excretion boys vs girls) graphically demonstrates a declining ability for the male children's kidneys to excrete mercury via the urine after the 2nd year of continued mercury exposure from their amalgam fillings. This may indicate that mercury exposure coupled with inability to excrete mercury is involved in the risk for autism as the ratio of boys to girls is about 4:1. The significant decrease in the boy's ability to excrete mercury is most likely due to kidney damage or to the natural increase in testosterone as they age which increases the cellular uptake and retention of mercury. Testosterone has been shown to increase the toxicity of mercury and thimerosal whereas estrogen has been shown to have a protective effect.

Barregard (attachment: Barregard, 2008) showed a "significantly increased prevalence of microalbuminuria in the children in the amalgam group (CAT study) in the years 3-5." This is consistent with increased kidney damage and not consistent with a conclusion of safety for dental amalgams as previously stated by the authors of the CAT studies.

Rose (attachment: Rose et al., 2008) suggests that children with autism who inherit the ALAD2 allele have lower glutathione levels and will be at increased risk for lead and mercury induced prenatal and postnatal developmental neurotoxicity due to the fact that glutathione is the natural molecule that binds and aids in the removal of mercury from the body. It is well known in the literature that exposure to mercury causes a rapid decrease in available glutathione.

Hagele, et al. (attachment: Hagele, 2007) showed that mercury activates phospholipase D (PLD) in the vascular epithelium and blood , suggesting an important initiating role in cardiovascular disease. The activation of this enzyme system may be induced by the constant mercury exposure from dental amalgam and represents a significant risk for both genders and all age groups.

3. Summary:

Mercury is one of the best known and most potent of neurotoxins to which humans are commonly exposed, especially with the presence of dental amalgams inches from the brain releasing mercury vapor which crosses the blood-brain barrier with ease. **With the current history of neurological disorders increasing in our nation's children it seems reasonable to take every precaution to decrease exposures to mercury by eliminating dental amalgam**. Taking into account that it is the *retention* of mercury in the different organs of the body and especially the brain that causes illnesses, all mercury exposures need to be reduced if possible. It is important to note that the ADA spokespersons base their opinion on amalgam safety based totally on mercury levels in the blood, urine or hair. Recent science has shown that these are not measures of total exposure or body burden but likely represent a combination of exposure and the excretion ability of the individual. This is confirmed by the fact that young men who die of idiopathic dilated cardiomyopathy have 178,400ng Hg/g of heart tissue compared to 8ng Hg/g for controls (Attachment: IDCM slide) - yet no data exists that finds these mercury levels in excretory fluids. This immense concentration of mercury in the heart tissue of young men may be due to their elevated testosterone levels and contributes to the complexity of any claims of a safe mercury exposure level based solely on urine, hair or blood levels.

The EPA, NAS and many other prestigious organizations have worked tirelessly to eliminate mercury exposures to humans and the environment. In fact, the EPA and the NAS have put in their comment that "about 8 to 10% of American women have such high mercury levels as to render susceptibility to neurological illnesses any child they would give birth to." Recently, in New York City, this level has risen to about 25%. The CDC has stated that 1 in 6 children in the USA currently suffers from some sort of neurological illness. These are major concerns, and it is obvious that mercury would exacerbate any neurological illnesses due to its neurotoxic properties. Therefore it seems prudent to implement a policy through the FDA to eliminate an exposure to

mercury vapor that exists inches from the brain, and which continuously releases mercury vapor - against which the human brain has no barrier.

The FDA requires dental/medical devices to exhibit "Reasonable Assurance" of safety and effectiveness. Specifically, 21CFR 860.7(d)(1) states " There is reasonable assurance that a device is safe when it can be determined, based upon valid scientific evidence, that the probable benefits to health from use of the device for its intended uses and conditions of use, when accompanied by adequate directions and warnings against unsafe use, outweigh any probable risks. The valid scientific evidence used to determine the safety of a device shall adequately demonstrate the absence of unreasonable risk of illness or injury associated with the use of the device for its intended uses and conditions of use." Amalgams, due to their easily proven release of mercury vapor do not suggest any safety in this regard at all. Therefore, the continued use of dental amalgam is not "reasonable" given the current state of the scientific literature of which only a small amount has been cited here. **It is our opinion that classification as Class II with special controls is clearly insufficient to provide reasonable assurance of safety. Neither "Class II controls" or "Special controls" can accomplish "reasonable assurance" of safety for all sectors of our general population. We are of the opinion that dental amalgam use in humans, because of its unacceptable risks to the public, especially to children and women of childbearing age, should be abolished, but at the very least be placed into Class III in the interest of public health and safety.**

Respectfully submitted by the Scientific Advisory Board for the International Academy of Oral Medicine & Toxicology.

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International Academy of Oral Medicine and Toxicology
Position Statement of the Scientific Advisory Board

In spite of its long term usage, accumulated scientific evidence now clearly shows that dental amalgam (silver-mercury fillings) expose dentists, dental staff members and dental patients to substantial amounts of mercury in vapor, particulate and other forms. Because chronic exposure to mercury, even in minute amounts, is known to be toxic and poses risks to human health, we must conclude that dental amalgam is not a suitable material for dental restorations.

Due to mercury's inhibiting influence on the growing brain, it is incompatible with current science and experimental knowledge to endorse or condone the use mercury containing fillings - especially in children and women of childbearing age.

Physicians and dentists should, where patients are suffering from pathological states and diseases of unclear causation, consider whether exposure to mercury released from amalgam fillings may be a contributory or exacerbating factor in such adverse health conditions.

Governments of other countries (e.g. Canada, the United Kingdom, Germany, France, Sweden, and Norway) have placed restrictions and/or issued advisories against the use of mercury in dental fillings - particularly in children and pregnant women. Recently a joint panel of FDA scientific advisors (1) rejected an FDA whitepaper's assurances of the safety of dental amalgam.

In light of the above mentioned facts, the International Academy of Oral Medicine & Toxicology and its Scientific Advisory Board (2) urge the dental profession to join the rest of the medical profession and abandon the use of mercury.

References:

(1) Joint Meeting of the Dental Products Panel of the Medical Devices Advisory Committee of the Center for Devices and Radiological Health, and the Peripheral and Central Nervous System Drugs Advisory Committee of the Center for Drug Evaluation and Research (September 6&7, 2006).

(2) Scientific Advisory Board

The scientific activities of the IAOMT are overseen by an advisory committee composed of world leaders in biochemistry, toxicology and environmental medicine. They are:

Boyd Haley, PhD, FIAOMT, chairman. Professor and former Chairman of the Department of Chemistry, University of Kentucky; permanent member, NIH Biomedical Sciences, Study Section.

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