



## **CRITIQUE OF THE CHILDREN'S AMALGAM STUDY CONSENT FORMS (American forms and Portuguese forms)**

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### **Summary of critique.**

The Children's Amalgam Study is an \$11 million study which began in 1997 to prove the "null hypothesis:" that mercury amalgam dental fillings do not cause adverse health effects in children. Approximately 500 American Children and 500 Portuguese children are study subjects. The Nuremberg Code, federal regulations (45 CFR 46 *et. seq.*) and common law require that study subjects or their parents/guardians give informed consent prior to commencing any study with associated risks.

While the American consent forms do disclose that the amalgams contain mercury, they do not disclose that these fillings are 50% elemental mercury. The consent forms do not disclose how much mercury exposure or absorption occurs from the fillings. There is no disclosure of previous study results which have revealed adverse affects to the human body and to animals from mercury amalgams. There is no disclosure of *in vitro* studies which elicit grave concern for the safety of mercury-emitting amalgam dental fillings. A significant number of the child-subjects are poor and/or minorities. The American subjects receive money for submitting to tests.

The Portuguese consent forms *do not disclose that the amalgams contain mercury*, nor do they disclose *any* risks associated with these fillings despite a large body of peer-reviewed scientific articles which reveal such risks. These children attend Casa Pia schools which includes orphans and handicapped children. The study investigators from the University of Washington indicate these children have been subjects for other studies in which the University has been involved.

In November 2002, the Portuguese press revealed a decades-long sex abuse scandal at the school. The international press in December 2003 revealed the indictment of 10 high profile Portuguese defendants charged with abuse. School administrators were involved in the facilitation of this abuse. While it is unknown whether any of the child-subjects were also victims of the scandal, the school environment had to be one of duress.

Preliminary results show that the Casa Pia children, as of March 2002, had 4.22 ug/l (micrograms of mercury per liter) of mercury in their urine. University of Washington researchers in 1998 published a peer-reviewed study showing that dentists with < 4 ug/l of mercury in their urine had adverse neuropsychological and neurobehavioral effects.



(While no preliminary results have been revealed for the American children, similar results would be expected.) Two more years of mercury exposure have occurred since these preliminary results were disclosed. Without a doubt, mercury levels in these children have continued to increase.

This critique finds that the informed consents used in this study are inadequate and invalid under the standards of the Nuremberg Code, federal regulations and common law. Dental therapy was not the primary purpose of this study. Its primary purpose is to justify the continued use of mercury amalgam by dentists even though it is well-known that mercury from the amalgam bioaccumulates and has been shown to be the primary source of mercury in the human body. The purpose of the study is to serve the economic purposes of dentistry.

Since at least March 2002, the investigators have known that the child-subjects have accumulated levels of mercury proven to cause neurological damage. The study must be terminated.

## **Introduction.**

The use of mercury in dental fillings has been controversial for over 150 years. The American Dental Association (ADA) was founded in 1859 by tradesmen (barbers and blacksmiths), who used mercury amalgam as a dental filling material. The Association of Dental Surgeons (ADS) was the ADA's competitor. Its members were medical doctors with a dental specialty. They used molten gold as a filling material. They also made their members sign a pledge agreeing not to use mercury as a dental filling material because they knew the toxicity of mercury and were familiar with the "Mad Hatter's disease" (mercury was used in the hat felting process).<sup>1</sup> As the ADA expanded, the ADS disappeared.

Despite a large body of scientific studies showing mercury to be a neurotoxin, a nephrotoxin, a cytotoxin and to adversely affect the human body,<sup>2</sup> the ADA, and federal agencies staffed with ADA dentists, have insisted that there is not enough evidence linking amalgams to a specific disease to reconsider the use of amalgam as a dental filling material.<sup>3</sup>

Due to the pressure from consumer groups and research scientists, and concern by federal agencies (USPHS,<sup>4</sup> USATSDR,<sup>5</sup> FDA<sup>6</sup>) there has been a call for more government-

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<sup>1</sup> <http://www.toxicteeth.org/mercfacts.cfm>

<sup>2</sup> <http://www.amalgam.org/#anchor59579> <http://home.earthlink.net/~berniew1/http://www.testfoundation.org/amalgam.htm>

<sup>3</sup> <http://www.ada.org> ; <http://www.fda.gov/cdrh/consumer/amalgams.html>

<sup>4</sup> U.S. Public Health Service

<sup>5</sup> U.S. Agency for Toxic Substances and Disease Registry



funded scientific studies. Since 1972 the National Institute of Dental and Craniofacial Research (NIDCR), an institute of the National Institutes of Health (NIH), has paid for more than 500 research grants related to amalgam efficacy and safety.<sup>7</sup> Of all of these studies, few have resulted in peer-reviewed published articles.<sup>8</sup> And simple, obvious studies have not been commissioned. Much would be revealed by a large study of people with and without amalgams. Those populations should be compared for general health status, neurological diseases, oral diseases, skin diseases, allergies, autoimmune diseases, kidney diseases, mental health and learning disabilities.

NIDCR, in 1997, issued a news release announcing a controlled clinical trial involving mercury amalgam. It acknowledged that there are “studies [which] have suggested that mercury-containing dental amalgams may be the cause of various diseases ranging from mild skin conditions to debilitating neuromuscular diseases.” Since 1997 the NIDCR has allocated \$11 million in grants for a two-part clinical trial to examine the health effects of mercury-containing dental fillings in children. It is called: “The Children’s Amalgam Study.”<sup>9</sup>

One part of the study is a joint effort between the University of Washington and the University of Lisbon, Portugal. The subjects are 500 children at the Casa Pia Schools in Portugal. The other part is a cooperative project between the New England Research Institutes, Forsyth Dental Center, Harvard Children’s Hospital and the University of Rochester. The subjects are children in urban Boston and children in rural Maine.

A question has arisen as to the adequacy of the consent forms used in the study. A review was conducted of the American consent form dated February 3, 2000, as well as of the Portuguese consent form dated January 28, 2000.<sup>10</sup>

### **Standards of consent for human experiments.**

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<sup>6</sup> Food and Drug Administration

<sup>7</sup> See, NIDCR CRISP database at: <http://crisp/crisp.cit.nih.gov/>; go to “Crisp inquiry;” use keyword “amalgam”, use NIDCR database for 1972-2004 to generate 538 “hits” of NIDCR-funded studies related to amalgam.

<sup>8</sup> The only peer-reviewed study on amalgam funded by NIDCR which has been published in the last decade is: Kingman, A., *Mercury concentrations in urine and whole blood associated with amalgam exposure in a US military population* J Dent Res. 1998 Mar;77(3):461-71. The authors’ conclusion was that while there was an increase in mercury levels of urine in military men with amalgams, there were no observable adverse effects. In fact, the study shows that men with amalgams have four times the amount of mercury in their urine as those without amalgam and that the level (approximately 4 ug/l) was the same level that *Echeverria, et al* demonstrated resulted in impairment in the Intentional Hand Steadiness Test, mental concentration, emotional lability, somatosensory irritation and mood. See cite at footnote 24.

<sup>9</sup> <http://www.clinicaltrials.gov/ct/show/NCT00065988?order=14>

<sup>10</sup> The study began in 1997 and presumably an earlier version of these forms exist which would require an independent analysis.



A fundamental legal and moral requirement for all medical trials is the informed consent of the subjects in the trial. Post World War II saw the birth of the Twentieth Century human rights movement. The Allies prosecuted surviving Nazi war criminals in an international military tribunal in Nuremberg, Germany, before international judges. The Doctors Trial presented evidence of murder and torture under the guise of medical experimentation.<sup>11</sup> The court's final judgment of the 23 medical doctor defendants articulated the Nuremberg Code (The Code), a 10-point statement of rules designed to protect the rights and welfare of research subjects.<sup>12</sup> The first, and primary rule is:

*The voluntary consent of the human subject is absolutely essential.*

The Nuremberg Code remains the seminal document guiding the principles that must be applied to human experimentation. In 1964 these principles were incorporated by the World Medical Association in its *Declaration of Helsinki: Recommendations Guiding Medical Doctors in Biomedical Research Involving Human Subjects*,<sup>13</sup> which made further distinctions between therapeutic and non-therapeutic research.

The NIH also incorporated these principles in 1966 as the *Policies for the Protection of Human Subjects*, which became regulations in 1974.<sup>14</sup>

In 1981, the "basic regulations" for the Department of Health and Human Services (DHHS) were codified at Title 45 Part 46 of the CFR. They apply to the 16 federal agencies that regulate human research. FDA has also adopted some of its provisions.<sup>15</sup>

In 1983, subpart D was added to these regulations and is entitled: *Additional Protections for Children Involved as Subjects in Research*. These provisions were intended to protect children as a specially identified vulnerable population.

These regulations were amended in 1991 and again in 2001 and are now identified as: *Federal Policy for the Protection of Human Subjects (Basic DHHS Policy for Protection of Human Research Subjects)*.<sup>16</sup>

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<sup>11</sup> Slide presentation on website for Data and Safety Monitoring Board (DSMB) on human experiments of history.  
<http://www.icssc.org/Final%20presentations%20for%20CD/04%20Historical%20and%20Ethical%20Perspectives.pdf> .

<sup>12</sup> *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10, Vol. 2, pp. 181-182.* Washington, D.C.: U.S. Government Printing Office, 1949.  
<http://ohsr.od.nih.gov/nuremberg.php3>

<sup>13</sup> Revised in 1975 and 1989. [http://ohrp.osophs.dhhs.gov/irb/irb\\_introduction.htm](http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm)

<sup>14</sup> [http://ohrp.osophs.dhhs.gov/irb/irb\\_introduction.htm](http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm)

<sup>15</sup> Title 21 Parts 50 and 56 of the CFR. Part 860 (Medical Device Classification Procedures) is also relevant.

<sup>16</sup> [http://ohrp.osophs.dhhs.gov/irb/irb\\_introduction.htm](http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm)



Another important historical document, from 1978, which was used as guidance by the federal agencies involved in human research, and matured their protective approach to human experiments, is: *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research*.<sup>17</sup> It is a report which was submitted by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The report sets out three principles as the “quintessential requirements for the ethical conduct of research involving human subjects:” (1) respect for persons, (2) beneficence; and, (3) justice.

In light of the child-subjects in the Children’s Amalgam Study, “justice” is especially salient. Justice in the realm of human research requires that the “benefits and burdens of research be distributed fairly.”<sup>18</sup> That includes a fair selection procedure of research subjects.

Federal regulations require that each institution conducting research create an Institutional Review Board (IRB) to assure compliance with 45 CFR 46 et. seq.<sup>19</sup> The *Institutional Review Board Guidebook*, in its Introduction, explains the requirement for “Justice” as follows:

*...The “justness” of subject selection relates both to the subject as an individual and to the subject as a member of social, racial, sexual, or ethnic groups.*

*With respect to their status as individuals, subjects should not be selected either because they are favored by the researcher or because they are held in disdain (e.g. adults before children) and that some classes of potential subjects (e.g., the institutionalized mentally infirm or prisoners) may be involved as research subjects, if at all, only on certain conditions.*

*Investigators, institutions, or IRBs may consider principles of distributive justice relevant to determining the appropriateness of proposed methods of selecting research subjects that may result in unjust distributions of the burdens and benefits of research. Such considerations may be appropriate to avoid the injustice that “arises from social, racial, sexual, and cultural biases institutionalized in society.”*

*Subjects should not be selected simply because they are readily available in settings where research is conducted, or because they are “easy to manipulate as a result of their illness or socioeconomic conditions.” Care should be taken to*

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<sup>17</sup> September 30, 1978.

<sup>18</sup> [http://ohrp.osophs.dhhs.gov/irb/irb\\_introduction.htm](http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm)

<sup>19</sup> The IRB is a review board charged with protecting human subjects from harm in National Institutes of Health research studies. <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>.



*avoid overburdening institutionalized persons who “are already burdened in many ways by their infirmities and environments.” Non-therapeutic research that involves risk should use other, less burdened populations, unless the research “directly relate[s] to the specific conditions of the class involved.”<sup>20</sup>*

The informed consent forms used for the Children’s Amalgam Study fall far short of the mandates of The Code, the legal requirements of federal regulations, as well as common law. While there were two very different consent forms used for the American children and the Portuguese children, both are inadequate to meet the requirements of an informed consent.

### **The American Consent Forms.**

The American consent forms include a five-page form for the parents or guardians and a separate two-page consent form for the child-subject.<sup>21</sup>

*(1) Parental Consent Form.* Amalgam dental fillings are generally 50% elemental mercury, 25-35% silver and varying percentages of tin, copper, zinc and sometimes other metals.<sup>22</sup> This basic information is not disclosed anywhere in the consent form. The specific formulation of the amalgam to be used in the study is not disclosed, nor is the brand name of the product.<sup>23</sup>

The consent form however, does set out the purpose of the study as follows:

*(1) To measure the amount of exposure to mercury in children with dental amalgam (silver fillings) and to compare these measurements to those from children with other types of fillings, in this case, dental composite (white fillings) and stainless steel crowns; (2) To determine whether specific health effects that could be related to mercury occur in the group of children with dental amalgam more often than in the group of children with other types of fillings.*

The consent form obliquely discloses that amalgam contains mercury, but does not reveal that it is the primary component and comprises 50% of the filling.

The consent form discloses that “mercury in *large* amounts can cause health problems” and describes the serious health problems related to such exposures (tremors, memory

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<sup>20</sup> *Id.*

<sup>21</sup> Copies of these consent forms are available, upon request, from Consumers for Dental Choice, [Barbara@toxiceeth.org](mailto:Barbara@toxiceeth.org).

<sup>22</sup> For example, <http://www.caulk.com/index.html> (DFU/MSDS; category: “alloys”; keyword: “Dispersalloy”).

<sup>23</sup> On February 15, 2003, Dr. Timothy DeRouen, principal investigator for the Casa Pia arm of the study, disclosed to the King County Board of Health that the amalgam used in both the Portuguese children and the American children was Dispersalloy.



loss, insomnia, fatigue, headaches, irritability, slow nerve conduction, appetite loss and kidney problems). However, the consent form then inaccurately claims that there “is no evidence that any of these health effects happen with the *small* amounts of mercury from dental fillings.”<sup>24</sup> (Emphasis added.)

The consent form does not explain what quantity of mercury is “large” or “small.” It does not disclose the amount of mercury exposure from an average mercury amalgam dental filling. The World Health Organization (WHO), in a 1991 report, disclosed the amount of mercury absorbed by the body in the average person with amalgams as ranging between 3-17 ug (micrograms) per day.<sup>25</sup>

The consent form explains that:

*“...because of the concern that small amounts of mercury are being released from amalgam fillings all the time and that this mercury might accumulate in the body...[the Children’s Amalgam Study is intended to] ... thoroughly investigate the amount and possible effects of mercury exposure from dental amalgam...”*  
(Emphasis added.)

In truth, those “concerns” have been raised by peer-reviewed scientific studies, as well as the WHO report which concluded that mercury from amalgams was bioavailable and bioaccumulating in human bodies. WHO also concluded that amalgam was the primary source of human mercury body burden. (WHO Criteria #118, p. 36 [1991]).<sup>26</sup>

The consent form contains a page and a half of protocols, procedures and schedules of the trial.

On page 3 of the consent form there is a paragraph entitled: “Risks/Mitigation.” It informs the parents that their child has a 50% chance of being in the amalgam group “with the risk of low level mercury exposure.” The form assures the parents that dental amalgam “is currently the most frequently used material to fill cavities in the back teeth...” That statement is followed by the odd and threatening statement that: “...if I choose to not participate in this study, it is very likely that my child’s teeth will be filled with amalgam by another dentist.”

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<sup>24</sup> See, Echeverria, D. *Neurobehavioral effects from exposure to dental amalgam Hg(o): new distinctions between recent exposure and Hg body burden*, FASEB J. 1998 Aug;12(11):971-80 (presents convincing new evidence of adverse behavioral effects associated with low mercury exposures within the range of that received by the general population from mercury amalgams); [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9707169&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9707169&dopt=Abstract)

<sup>25</sup> <http://www.inchem.org/documents/ehc/ehc/ehc118.htm> (Section 5.1.1.1 [Table 2])

<sup>26</sup> The WHO document states that the average person with amalgam fillings who eats fish absorbs 3-17 ug/day of mercury from amalgams; 2.3 ug/day from fish; 0.03 ug/day from air; and, 0.0035 ug/day from water. <http://www.inchem.org/documents/ehc/ehc/ehc118.htm> (Section 5.1.1.1 [Table 2])



Such a statement makes the economic circumstances of the parents relevant. If these parents are low income, their children truly do not have a choice of dental filling materials. Amalgam is cheap and easy for the dentist to place and is generally the only choice available to those on Medicaid.<sup>27</sup> Middle class white parents are choosing composites over amalgam for their children. A large percentage of the child-subjects are low income and/or minority children.<sup>28</sup> The availability of free dental care through this study to offset dental costs is coercive, pitting the parents' financial pressures against the child's welfare.

The consent form then purports to disclose the risks of the composite fillings. It does not identify by chemical name or brand name the material which will be used. The form states that:

*“...sometimes the dental composite releases a chemical in the mouth which in much larger amounts may cause cancer. However, this filling material is currently the standard material used to fill cavities in the front and many back teeth, and no one has ever reported a problem with dental composite.” (Emphasis added.)*

This statement is coercive – leading parents to have fewer objections to having their child in the mercury amalgam group. And, if indeed, the composite material being used in this trial contains chemicals that may cause cancer, it is unethical in light of the fact that there are composites which are non-toxic based on the ADA/ANSI toxicity scale.<sup>29</sup> There are also studies which indicate that many problems with composites *have been reported*,<sup>30</sup> but they are not disclosed in this consent form.

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<sup>27</sup> In 2003 the State of California passed a law allowing Medicaid patients a choice of dental filling materials and authorizing reimbursements to dentists placing non-amalgam filling materials (AB 999). In other states those on Medicaid get mercury amalgam dental fillings or nothing.

<sup>28</sup> A December 12, 2003, PowerPoint presentation by Dr. Daniel Bellinger to an FDA/NIDCR mercury amalgam scientific panel, disclosed the demographics of the child-subjects. 50% of their families earn under \$30,000 per year. 37% are minority children. There was no disclosure of the percentage of minority residents in urban Boston area or rural Maine to compare to this figure.

[http://www.lsro.org/presentation\\_files/amalgam/2003\\_12\\_12/bellinger.ppt](http://www.lsro.org/presentation_files/amalgam/2003_12_12/bellinger.ppt)

<sup>29</sup> <http://www.biodent.com.au/biocompatibility.html>

<sup>30</sup> A. Franz, *Cytotoxic effects of packable and nonpackable dental composites*, Dent Mater. 2003 Jul; 19(5):382-92

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12742433&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12742433&dopt=Abstract) ; Janke V, *TEGDMA causes apoptosis in primary human gingival fibroblasts*, J Dent Res. 2003 Oct;82(10):814-8.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=14514762&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14514762&dopt=Abstract) ; W. Geurtsen, *Cytotoxicity of 35 dental resin composite monomers/additives in permanent 3T3 and three human primary fibroblast cultures*, J Biomed Mater Res. 1998 Sep 5;41(3):474-80

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9659618&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9659618&dopt=Abstract) ; and, Scarano A, *Direct capping with four different materials in humans: histological analysis of odontoblast activity*, J Endod. 2003 Nov; 29(11):729-34





The remainder of the risks disclosed in the consent form relate to the injected anesthesia and pain from blood collection.

On page 4 of the consent form there is a paragraph entitled: “Benefits” which promises the child-subjects high quality dental care for 5 years and blood test results which will be provided to the child’s pediatrician at no cost. The consent form also promises to pay the child \$20 per visit for non-dental visits.<sup>31</sup> Again, with low income children, this is coercive. Parents may seek participation for their children to obtain this small, but perhaps significant, cash award.

The consent form requires the parent to waive claims for injuries from the study treatments other than immediate emergency care.

The parental consent form is wholly inadequate. The 10-point Code statement, limiting permissible medical experimentation on human subjects, provides the standards for an valid consent. The analysis below demonstrates the inadequacy of the parents’ consent form for the American children:

***The Code, Point #1*** states that:

*The voluntary consent of the human subject is absolutely essential.*

*This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment.*

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=14651279&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=14651279&dopt=Abstract) .

<sup>31</sup> According to Dr. Daniel Bellinger, a psychologist associated with Harvard University, who is evaluating some of the child-subjects for IQ changes, the child-subjects are now receiving \$50 per visit for non-dental visits. Bellinger testified to this increased payment on December 12, 2003, before an FDA/NIDCR scientific panel which is reviewing recent scientific journal articles on the safety and efficacy of mercury amalgam dental fillings. *Personal communication with Charles G. Brown, Esq., Consumers for Dental Choice, Washington, D.C., December 13, 2003, who heard Dr. Bellinger’s testimony.*



*The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity. (Emphasis added.)*

This consent form does not meet the letter or spirit of this provision of The Code. This consent form gives parents a choice of: (a) mercury-containing amalgams in the study; (b) mercury-containing amalgams from another dentist outside the study; or, (c) composite fillings in the study which contain cancer-causing chemicals. This consent form is not an exercise of free power of choice, especially for those families with the least resources. The parents are under duress because they must choose between no dental care or dental care on the study investigators' terms without true disclosure of all the risks. The consent form is also deceitful because it does not disclose the amount of mercury in the amalgam or the toxic components of the composite fillings.

The Code requires that the parents be given sufficient knowledge of the subject matter and that they understand the information to make an enlightened decision. This consent form leads a parent to believe the amalgam fillings must be safe because they are "widely used."<sup>32</sup> It tells parents that amalgam is only one of the sources of mercury exposure in addition to food, water and air, but fails to disclose amalgam is the *primary source* of human mercury body burden in people with amalgam fillings while the amounts from air and water are negligible.<sup>33</sup>

Despite the requirement that the consent form disclose every *possible* effect on the health of the subject from the experiment, the consent form does not disclose *any* risks from chronic low-level mercury exposures which have been documented to cause impairment in the Intentional Hand Steadiness Test, mental concentration, emotional lability, somatosensory irritation and mood.<sup>34</sup> The consent form does not disclose that amalgams cause periodontal disease.<sup>35</sup> Periodontal disease, in turn, has been linked to cardiovascular disease,<sup>36</sup> diabetes,<sup>37</sup> preterm birth and low birth weight.<sup>38</sup> The consent form does not disclose that the mercury in amalgam has been linked to antibiotic resistant mouth and gut bacteria.<sup>39</sup> The consent form does not disclose that mercury in amalgam

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<sup>32</sup> Amalgam has never been determined to be safe and effective. FDA Dental Devices Division has jurisdiction over amalgam. FDA has not approved amalgam for safety; it has not required manufacturers of amalgam to prove that amalgams are safe. Instead, \$11 million of taxpayer money is being used to provide the evidence that amalgams do not cause adverse health effects.

<sup>33</sup> WHO Criteria # 118, p. 36 (1991); <http://www.inchem.org/documents/ehc/ehc/ehc118.htm> (Section 5.1.1.1 [Table 2]).

<sup>34</sup> Echeverria, <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=PubMed> ; keyword: "Echeverria D", articles (2), (3) and (6).

<sup>35</sup> <http://www.toothwisdom.net/p.mercury&gums.html>

<sup>36</sup> <http://www.thejcdp.com/issue001/paquette/7paq.htm>

<sup>37</sup> [http://www.umich.edu/~urecord/9899/Jan25\\_99/gums.htm](http://www.umich.edu/~urecord/9899/Jan25_99/gums.htm)

<sup>38</sup> <http://www.saveyoursmile.com/healthygums/prematurebirths.html>

<sup>39</sup> <http://www.uga.edu/cms/FacAOS.html>



has been linked to immune suppression and autoimmune disease.<sup>40</sup> The consent form does not disclose that amalgam has been linked to oral *lichen planus* (mouth mucus membrane lesions) and when the amalgam is removed most cases are resolved.<sup>41</sup>

The Code of Federal Regulations (CFR) sets out the general requirements for informed consent for federally funded experiments. 45 CFR 46.116. These requirements include those listed in Point 1 of The Code. Of the mandatory components of the informed consent form, two are particularly pertinent here:

- (1) A description of any reasonably foreseeable risks or discomforts to the subject; and,
- (2) A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

Since this study involves exposure to mercury, which is undisputedly the most toxic of the heavy metals,<sup>42</sup> that risk must be disclosed. The quantity of mercury to which the subject would be exposed should also have been disclosed. At the commencement of this study, the WHO had already quantified the exposure at 3-17 ug/day, more than the Environmental Protection Agency (EPA)<sup>43</sup> and US Agency for Toxic Substances and Disease Registry (USATSDR)<sup>44</sup> safety levels for children. These safety limits also should have been disclosed. The WHO has concluded that a safe level of mercury exposure, below which no adverse effects occur, has never been established.<sup>45</sup> This risk should also have been disclosed. The studies showing adverse effects from low level, chronic mercury exposure should have been revealed as well (as set forth above).

The failure to disclose that there are safe composite filling materials,<sup>46</sup> which are “appropriate alternative procedures” violates the requirement to disclose such alternative

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<sup>40</sup> Kim, SH, et al, *Oral exposure to inorganic mercury alters T lymphocyte phenotypes and cytokine expression in BALB/c mice*, Arch Toxicol. 2003 Nov;77(11):613-20. Epub 2003 Aug 20; and, Mirtcheva, J, et al, *Immunological alterations inducible by mercury compounds. III. H-2A acts as an immune response and H-2E as an immune "suppression" locus for HgCl<sub>2</sub>-induced antinucleolar autoantibodies*, Eur J Immunol. 1989 Dec;19(12):2257-61.

<sup>41</sup> Wong, L, et al, *Oral lichenoid lesions (OLL) and mercury in amalgam fillings*. *Contact Dermatitis*, 2003 Feb;48(2):74-9.

<sup>42</sup> See, footnote # 67, *infra*. (mercury is 40 times more toxic than lead).

<sup>43</sup> The EPA health standard for elemental mercury vapor exposure is 0.3 mcg per cubic meter of air which equates to 6 ug/day for the average adult; or, 0.1 ug/kg body weight per day or 6-7 ug/day for the average adult. The total amount for a child would be much less based on weight.

<sup>44</sup> USATSDR standard for inhalation exposure to mercury vapor is 0.2 mcg per cubic meter of air, which translates to 4-6 ug/day for the average adult.

<sup>45</sup> WHO document # 118, 1991. p. 21 (“a consequence of an immunological etiology is that, in the absence of dose-response studies for groups of immunologically sensitive individuals, it is not scientifically possible to set a level for mercury (e.g., in blood or urine) below which (in individual cases) mercury-related symptoms will not occur.” The Children’s Amalgam Study is not designed to identify immunologically sensitive individuals. <http://www.inchem.org/documents/ehc/ehc/ehc118.htm>

<sup>46</sup> [www.biodent.com.au/diamondlite.html](http://www.biodent.com.au/diamondlite.html) <http://www.biodent.com.au/biocompatibility.html>



treatments. Additionally, the failure to document compliance with 45 CFR 46.116 is a violation of 45 CFR 46.117 which requires a written informed consent form incorporating the elements of 45 CFR 45.116.

**The Code, Point 2**, requires that:

*The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*

The purpose of this Children's Amalgam Study is: "to document whether or not there are adverse health effects of mercury attributable to mercury-containing dental amalgams."<sup>47</sup> However, because safe alternative dental filling materials exist,<sup>48</sup> it is evident that the real purpose of the study is to show that amalgams do *not* produce evidence of health harm so that dentists can continue to use amalgam for their economic benefit (it is cheap and very easy to use).<sup>49</sup> Prior human studies and animal studies have shown mercury, as found in amalgams (mercury vapor, elemental inorganic mercury ions and methylated organic mercury), is harmful to all cells,<sup>50</sup> enzymes,<sup>51</sup> hormones,<sup>52</sup> proteins,<sup>53</sup> and neurons.<sup>54</sup>

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<sup>47</sup> NIDCR press release 1-8-1997.

<sup>48</sup> [www.biodent.com.au/diamondlite.html](http://www.biodent.com.au/diamondlite.html) [www.biodent.com.au/biocompatibility.html](http://www.biodent.com.au/biocompatibility.html)

<sup>49</sup> See statement by Dr. Tavares, a Co-principal investigator, who describes the "null hypothesis" of this study as showing no difference in IQ from baseline to the end of the trial between the amalgam group and the composite group. *Infra*, at page 16. Dr. Tavares also admits that there will be a "small change" in "renal outcomes [which] are not well understood." It would probably be safe to conclude that those changes are adverse to the health of the child-subjects, and not helpful. The manufacturer of Dispersalloy amalgam has disclosed that it is a known nephrotoxin (toxic to the kidneys).

<sup>50</sup> Bahia, Mde O., *Genotoxic effects of mercury on in vitro cultures of human cells.*

An Acad Bras Cienc. 1999;71(3 Pt 1):437-43.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10530333&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10530333&dopt=Abstract)

<sup>51</sup> Watanabe C, *In utero methylmercury exposure differentially affects the activities of selenoenzymes in the fetal mouse brain.* Environ Res. 1999 Apr;80(3):208-14.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10092441&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10092441&dopt=Abstract)

<sup>52</sup> Facemire, CF, *Reproductive impairment in the Florida panther: nature or nurture?* Environ Health Perspect. 1995 May;103 Suppl 4:79-86,

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=7556029&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=7556029&dopt=Abstract)

<sup>53</sup> Olivieri G, et al, *Mercury induces cell cytotoxicity and oxidative stress and increases beta-amyloid secretion and tau phosphorylation in SHSY5Y neuroblastoma cells,* J Neurochem. 2000 Jan;74(1):231-6.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10617124&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10617124&dopt=Abstract)

<sup>54</sup> Sorensen, FW, et al, *Neuron loss in cerebellar cortex of rats exposed to mercury vapor: a stereological study,* Acta Neuropathol (Berl). 2000 Jul;100(1):95-100

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=10912926&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10912926&dopt=Abstract) ; Leong CC, et al, *Retrograde degeneration of neurite membrane structural integrity of nerve growth cones following in vitro exposure to mercury,* Neuroreport. 2001 Mar 26;12(4):733-7



*Fruitful results for the good of society?* If the result of this experiment is to prove, finally, to the dental industry that mercury amalgam is harmful to the human body and should no longer be used, that would be good for society even though bad for the child-subjects. If, on the other hand, the results have been preordained (that amalgams do *not* cause health harm) and evidence will be marshaled to support that desired result to justify the continued use of mercury amalgam, a great disservice to society will occur. The dental industry will then have a scientific study to support its continued placement of mercury in the mouths of dental consumers. Because much safer alternative filling materials already exist, society is harmed by the unethical exposure of these child-subjects to a known toxic substance.

*The information is unprocurable by other methods or means of study, and not random and unnecessary in nature.* The dental industry claims that the “gold standard” for a scientific study is a human double-blind controlled study. It acknowledges that the use of amalgam cannot be “double-blind” because the metal material is observable and distinguishable from the white composite filling used in the controls. Bias of the investigators who will be testing the child-subjects will necessarily be a concern. This study is being touted as the best scientific evaluation of potential harm from mercury in amalgam. The proponents of the study (the dental industry, FDA and NIDCR) discount prior studies which are said to be too small, not controlled, retrospective, on animals, *in vitro*, or subject to confounders. However, the very large body of peer-reviewed scientific studies to date have overwhelmingly proven that the mercury in amalgam is not inert, is absorbed by the body, interferes with cellular processes and affects all cells, hormones, enzymes, proteins and neurons.<sup>55</sup>

This clinical trial, which involves placing toxic mercury in children, is unethical in light of prior studies showing health harm and because of the inadequate consent form. Many minimum and maximum toxicant levels have been set by the federal government based upon animal studies because it would be unethical to experiment with humans to set toxic levels. EPA, U.S. ATSDR and Health Canada have set safety levels for mercury based on existing studies. As stated earlier, the EPA safety level is set at 7 ug/day for the average adult and the U.S. ATSDR health standard is 4-6 ug/day. Health Canada has a much more protective limit of 1 ug/day for the average adult. WHO Document # 118 shows that the average absorption of mercury exposure for amalgam can far exceed these daily limits (i.e. 3-17 ug/day).<sup>56</sup> And, in a large German study with 20,000 subjects tested at a university medical clinic, the average exposure from fillings was over 10

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=11277574&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11277574&dopt=Abstract) .

<sup>55</sup> <http://home.earthlink.net/~berniew1/> ; <http://www.testfoundation.org/amalgam.htm> ; footnotes 50-54.

<sup>56</sup> See footnotes 25, 26, 43, 44 and 45, *supra*.



ug/day and over 50% of all those with 6 or more amalgam fillings had daily exposure exceeding the EPA health guidelines.<sup>57</sup>

Further controlled animal studies in mammals could closely approximate the effect of mercury on the human body without subjecting children to this toxic metal.<sup>58</sup>

These children studies are wholly unnecessary since there are many safe and effective alternative dental fillings.<sup>59</sup> Furthermore, the harm of mercury is well-known and supported by a very large body of research.<sup>60</sup>

Based on the articulated “null hypothesis” of this study (that amalgams do not cause health harm),<sup>61</sup> it is reasonable to conclude that the proponents are hoping that the result of this study will trump all prior studies showing otherwise. If that occurs, the results of the Children’s Amalgam Study will be widely cited by pro-amalgam dental interests to support the continued use of amalgam - all other research to the contrary will be ignored.

Why is the dental industry so wedded to amalgam? Placement of composites is described as “technique sensitive” meaning it takes more skill than placement of amalgams which is akin to placing putty or spackle. Dental schools have only begun to teach the placement of composites in posterior teeth, which means many older dentists have never been trained to do such place composites. There is also fear that abandoning amalgam will be an admission that it is unsafe and loss of professional reputation and liability will follow.

Ease-of-use, economic interests and concern for reputation cannot justify use of children in an experiment which unnecessarily exposes them to toxic mercury.

***The Code, Point 3*** states that:

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<sup>57</sup> <http://www.xs4all.nl/~stgvisie/AMALGAM/EN/SCIENCE/tubingen.html>

<sup>58</sup> Two seminal studies on animals involved the placement of radioactive mercury amalgam fillings in sheep and monkeys. Within 30 days a scan of the animals showed mercury from the amalgams had been absorbed into body tissues, especially the kidney and liver. Hahn, LJ, et al, *Whole-body imaging of the distribution of mercury released from dental fillings into monkey tissues*, FASEB J. 1990 Nov;4(14):3256-60. Thus, the investigators know that the child-subjects are similarly accumulating mercury throughout their bodies with no way to measure those accumulations short of a biopsy or autopsy. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2227216&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2227216&dopt=Abstract) ; and, Hahn, LJ, et al, *Dental "silver" tooth fillings: a source of mercury exposure revealed by whole-body image scan and tissue analysis*, FASEB J. 1989 Dec;3(14):2641-6 (the study subjects in this article were sheep). [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=2636872&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2636872&dopt=Abstract)

<sup>59</sup> <http://www.biodent.com.au/diamondlite.html> <http://biodent.com.au/biocompatibility.html>

<sup>60</sup> <http://home.earthlink.net/~berniew1/> <http://www.testfoundation.org/amalgam.htm>  
<http://www.amalgam.org/#59579>

<sup>61</sup> See, footnote 49.



*The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.*

As noted above, based on prior human and animal studies, the anticipated result of this study is that harm to the human body will occur. Because there are safe and effective alternatives for tooth restorations, this study, which exposes children to toxic mercury for the benefit of the dental industry, not for the benefit of dental consumers, is completely unjustified.

**The Code, Point 4** states that:

*The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*

This study unnecessarily exposes children to mercury, which has been proven to cause many kinds of physical and mental injuries.<sup>62</sup> While these injuries may not be immediately observable in this five-year study,<sup>63</sup> amalgams add an increasing mercury burden, which increases the likelihood of future adverse health effects.

**The Code, Point 5** states that:

*No experiment should be so conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*

Again, there is a large body of evidence that mercury, including mercury from amalgams, causes a wide range of health harm including disabling injuries and premature death.<sup>64</sup> In 2002, George Kazantzis authored a survey of 40 years of research, as well as a review of a series of WHO proceedings which addressed mercury toxicity. His article, which was published in a peer-reviewed journal, concluded that it was not possible to set a level for mercury in blood or urine below which mercury-related symptoms will not occur.<sup>65</sup> This corroborated the 1991 WHO findings.<sup>66</sup>

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<sup>62</sup> <http://home.earthlink.net/~berniew1/> <http://www.testfoundation.org> <http://amalgam.org/#anchor59579>

<sup>63</sup> This study has also been described as a seven year study by Dr. Timothy DeRouen. February 15, 2003, before the King County Board of Health, Seattle, WA. Tape available from KCCTV.

<sup>64</sup> <http://home.earthlink.net/~berniew1/> <http://www.testfoundation.org> <http://amalgam.org/#anchor59579> ; see also footnote # 87.

<sup>65</sup> Kazantzis, G., *Mercury exposure and early effects: an overview*, Med Lav. 2002 May-Jun;93(3):139-47. [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12197264&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12197264&dopt=Abstract)

<sup>66</sup> See footnote # 45.



It is very clear that the experiment investigators are not serving as subjects in this study. This experiment should never have been commenced.

**The Code, Point 6** states that:

*The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem solved by the experiment.*

The risk of harm from mercury in dental amalgams far outweighs any benefit from this study. The primary benefit of amalgam is economic and it accrues primarily to the dental industry (dentists can place more fillings in a shorter period of time and the costs of the amalgam material is negligible). While there may be a small economic benefit to patients (possibly cheaper dental care), no one suggests substituting lead as a dental material because it is cheaper, because its harmful nature is universally understood. Mercury is at least 40 times more toxic than lead.<sup>67</sup>

The existence of safe and effective alternatives to mercury amalgam<sup>68</sup> make experiments with amalgam unnecessary, unethical and of *no* humanitarian importance.

**The Code, Point 7** states that:

*Proper preparation should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.*

There is no amount of preparation nor standard of facilities which can offset the potential harm from permanently implanting a material which is 50% elemental mercury into the human mouth.

**The Code, Point 8** states that:

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<sup>67</sup> Shubert et al., published a study in the J. of Toxicology and Environmental Health (V4:763-776, 1978), in which they injected rats with lead and mercury to determine the LD values (the amount required to kill a certain % of the rats). The LD 100 (amount that kills all the rats) was 7 micrograms Hg/kg for mercury and 280 micrograms Pb/kg or lead. Therefore, by direct injection into the rat mercury is 40 times more toxic than lead. The paper also quotes "It is interesting to note that a combination of the LD 1 of each metal is 100% fatal." That is, mixing together a solution of lead that killed 1 of 100 rats with a solution of mercury that killed 1 of 100 rats resulted in a solution of Pb/Hg that killed 100 of 100 rats. This is synergistic toxicity. This is why it is nearly impossible to define a "safe" level of mercury. This synergy is also seen with cadmium (cigarette smoke) and other heavy metals. *Personal communication, Boyd Haley, PhD, Chair, Chemistry Department, University of Kentucky, February 16, 2004.*

<sup>68</sup> <http://www.biodent.com.au/diamondlite.html> <http://www.biodent.com.au/biocompatibility.html>





*The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment. (Emphasis added.)*

There are investigators and dental providers involved in this study. The investigators, whose identities were disclosed in the consent form, include:

Sybil Crawford, PhD, New England Research Institutes, *Original* Principal Investigator.<sup>69</sup> She has a BS in Economics and a PhD in statistics. She is listed as an author on 32 studies in PubMed; she is the lead author on 6 of them. Her primary areas of research have been menopause, ethnic differences in health care and statistical techniques. The New England Research Institutes is a “public health research facility” that began in 1986. Its motto is: “No research without therapeutic or policy benefit.” Much of its research is funded by the National Institutes of Health. It also contracts with corporations for studies, including pharmaceutical companies, biotechnology firms and dental product manufacturers seeking the ADA “Seal of Acceptance.”<sup>70</sup> (Dr. Crawford has been replaced as Principal Investigator and a web search shows Dr. Crawford is now on the faculty of the University of Massachusetts, School of Medicine.)

Mary Tavares, DMD, MPH, Forsyth Institute, Co-Principal Investigator. In a presentation to the FDA/NIDCR mercury amalgam scientific panel on December 12, 2003, Dr. Tavares is identified as the principal dental investigator.<sup>71</sup> She is the Associate Clinical Investigator for the Forsyth Institute, Department of Clinical Trials. She has a BA in Sociology, a DMD from Tufts and an MPH from Harvard School of Public Health. Dr. Tavares describes the Children’s Amalgam Study as a study which: “...should help to settle a controversy that has continued since the 1970’s.” She states that the “null hypothesis” of the study is that there will be no difference in IQ from baseline at the end of the trial between the amalgam group and the composite group. As a secondary endpoint there is an anticipated “small change” in “renal outcomes [which are] not well understood.”<sup>72</sup> This means that the investigators have decided the ultimate outcome of the study (amalgam is safe) and have concluded adverse impacts on the kidneys of the children are acceptable because such an outcome is “not well understood.” Dentsply, an

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<sup>69</sup> The PowerPoint presentation made to the FDA/NIDCR mercury amalgam scientific panel on December 12, 2003, sets out the names and affiliations of the Children’s Amalgam Study investigators. Sylvia Crawford is no longer listed as the Principal Investigator, Dr. Sonja McKinlay is listed instead.

<sup>70</sup> <http://www.neri.org/html/about/who/meet.asp>

<sup>71</sup> [http://www.lsro.org/presentation\\_files/amalgam/2003\\_12\\_12/bellinger.ppt](http://www.lsro.org/presentation_files/amalgam/2003_12_12/bellinger.ppt)

<sup>72</sup> [http://www.forsyth.org/re/re\\_i\\_tavares.htm](http://www.forsyth.org/re/re_i_tavares.htm)



amalgam manufacturer, has unambiguously warned that amalgam is a nephrotoxin (toxic to kidneys).<sup>73</sup> Placing amalgam in children is unethical.

Non-disclosed investigators include:

Sonja M. McKinlay, Ph.D, of New England Research Institutes, *Replacement* Principal Investigator.<sup>74</sup> Dr. McKinlay and John McKinlay founded the New England Research Institutes in 1986. They presently have over 200 employees. Dr. McKinlay's areas of expertise are statistics and epidemiology. She is listed as the author of 58 articles in PubMed.

Daniel Bellinger, PhD, Harvard University. Dr. Bellinger is a neuropsychologist who will be testing some of the New England child-subjects. IQ is one of the standards that he will be assessing.

David B. Daniel, PhD, Department of Psychology, Associate Research Scientist, University of Maine at Farmington, New England Research Institutes.<sup>75</sup> Dr. Daniel is a neuropsychologist and will be testing child-subjects.

Thomas W. Clarkson, PhD., is presently associated with the University of Rochester. He has been a Professor of Environmental Medicine, as well as a Professor of Biochemistry & Biophysics, and Pharmacology & Physiology. He was awarded a B.S. in 1953, and a Ph.D. in 1956 (University of Manchester). He is listed on a PowerPoint presentation to the FDA/NIDCR mercury amalgam scientific panel on December 12, 2003, as an investigator in the Children's Amalgam Study under the heading: "Exposure." Dr. Clarkson has 184 articles attributed to him in PubMed. He has extensive experience in mercury research, especially methylmercury. In a recently published article in which Dr. Clarkson was the lead author,<sup>76</sup> the authors concluded:

*"Patients who have questions about the potential relation between mercury and degenerative diseases can be assured that the available evidence shows no connection."*

However, this review article has been roundly criticized because it is predicated on a dose/response theory.<sup>77</sup> A recently published scientific peer-reviewed study indicates that those children who excrete the least mercury are the most affected because of

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<sup>73</sup> A copy of the 1997 Dentsply "Directions For Use" can be obtained from Consumers for Dental Choice, [Barbara@toxicteeth.org](mailto:Barbara@toxicteeth.org).

<sup>74</sup> See footnote 69.

<sup>75</sup> Contact information for Dr. Daniel: 234 Main Street, Farmington, ME, 04938, 207-778-7411, [dbdaniel@maine.edu](mailto:dbdaniel@maine.edu)

<sup>76</sup> Clarkson, TW, et al, *The Toxicology of Mercury - Current Exposures and Clinical Manifestations*. NEJM, 349(19):1731-1737, Oct 2003. <http://www.bioprobe.com/ReadNews.asp?article=72>

<sup>77</sup> <http://www.bioprobe.com/ReadNews.asp?article=72>



mercury tissue retention.<sup>78</sup> Dr. Clarkson also seems to have had a change in position about the dangers of mercury, especially “dental mercury.” See Dr. Clarkson’s earlier articles: *Toxicity Assessment of Mercury Vapor from Dental Amalgams*<sup>79</sup> in which the authors state:

*In conclusion, the evidence to date indicates that a substantial amount of dental amalgam Hg [mercury] vaporizes into mouth air, the Hg vapor is inhaled and swallowed, and significant concentrations of this Hg are distributed in body tissues resulting in alteration of cell function. Blood and urine Hg levels remain relatively low during amalgam Hg exposure, and therefore may be poor diagnostic indicators of the very high Hg levels that accumulate in some body tissues as a consequence of such exposure.*

Another relevant Clarkson study is: *Maximum Allowable Concentrations (MAC) of Mercury Compounds: Report of an International Committee*<sup>80</sup> in which the authors conclude:

*In view of the present knowledge about mechanisms responsible for mercury concentration in the blood and urine, a close correlation between them and the concentration in any critical organ should not be expected. Thus, in an individual case neither urine nor blood may indicate the degree of risk of intoxication.*

And in: *Workshop: Biocompatibility of Metals in Dentistry*<sup>81</sup>, Dr. Clarkson concluded:

*The distribution of mercury into body tissues is highly variable and there appears to be little correlation between levels in urine, blood or hair, and toxic effects.*

Lars Barregard, PhD, University of Goteberg, is listed as an investigator for the Children’s Amalgam Study on the New England Research Institutes website. His role is to measure renal function in the child-subjects. Dr. Barregard is listed as an author on 59 articles in PubMed. In one study looking at the levels of mercury, cadmium and lead in living, healthy Swedish subjects, the authors concluded that: “*The effect of dental amalgam on kidney Hg was as expected.*”<sup>82</sup> It leads one to conclude that the researchers expect harm to the kidneys of the children-subjects, but that does not dissuade them from proceeding with the experiment. Note that Dr. Tavares, above, makes the same observation with little concern.

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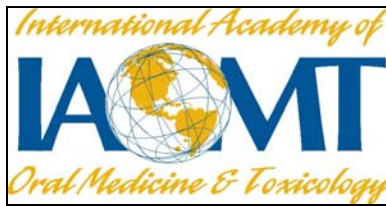
<sup>78</sup> Holmes, AS, *Reduced levels of mercury in first baby haircuts of autistic children*, Int J Toxicol. 2003 Jul-Aug;22(4):277-85.

<sup>79</sup> Goering, PL; Clarkson, TW, et al *Fundamental and Applied Toxicology*, Pg. 323, 19:319-29, 1992.

<sup>80</sup> Clarkson TW, et al, Arch Environ Health, 19:891-905, pg. 894 Dec 1969.

<sup>81</sup> NIDR, J American Dent. Assoc., 109:469-71, Sep 1984, p. 470.

<sup>82</sup> Barregard, L, et al, *Cadmium, mercury, and lead in kidney cortex of the general Swedish population: a study of biopsies from living kidney donors*, Environ Health Perspect. 1999 Nov;107(11):867-71.



Bruce Shenker, PhD, University of Pennsylvania Dental School, is listed as an investigator for the Children's Amalgam Study on the New England Research Institutes website. His role is identified as "Immune." PubMed credits him with 59 published articles and 16 articles related to the word "immune." Dr. Shenker's work includes studies of the effect of mercury on the immune system. A study of Dr. Shenker's, published in 2002, postulates that: "*There is growing evidence that heavy metals, in general, and mercurial compounds, in particular, are toxic to the human immune system.*"<sup>83</sup> The authors state what they already know: that methylmercury kills T-cells (a critical part of the immune system) and kills the mitochondria in cells. This study showed that methylmercury: decreases mitochondrial transmembrane potential; depletes the thiol reserves of the cells; depletes glutathione levels in the cells; causes oxidative stress activating cell death-signaling pathways; and, acts as a genotoxin significantly altering the expression of genes that affect cell survival and apoptosis (cell death).<sup>84</sup> Knowing all this, and continuing to place mercury in the mouths of the children-subjects is troubling.<sup>85</sup>

Felicia Trachtenberg, PhD, New England Research Institutes, was listed as an investigator for biostatistics in the presentation made by Dr. Bellinger to the FDA/NIDCR mercury amalgam scientific panel on December 12, 2003. She has four articles published in PubMed relating to genetic markers of ethnic populations.

Other than Dr. Clarkson and Dr. Shenker, none of these researchers, apparently, have any expertise in the biochemistry of mercury on the human body. This at least raises the question as to why these particular investigators were chosen for this assignment. Furthermore, the consent form does not identify the dentists who will be performing the

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<sup>83</sup> Shenker, BJ, et al, *Mercury-induced apoptosis in human lymphocytes: caspase activation is linked to redox status*, Antioxid Redox Signal. 2002 Jun;4(3):379-89.

<sup>84</sup> *Id.*

<sup>85</sup> Pro-amalgamists try to dismiss the importance of inorganic mercury from dental fillings as a toxic source by pointing to all the studies which show the organic form of mercury (methylmercury) to be the toxin of greater concern. However, it is clear that the mercury from amalgam is methylated by mouth and body bacteria. Heintze et al, *Methylation of Mercury from dental amalgam and mercuric chloride by oral Streptococc.*, Scan. J. Dent. Res. 1983, 91:150-152; Rowland, et al, *The Methylation of Mercuric Chloride by Human Intestinal Bacteria*, Experientia. Basel 1975 ,31: 1064-1065; L. Bjorkman et al, *Mercury in Saliva and Feces after Removal of Amalgam Fillings*, Toxicology and Applied Pharmacology, 1997, 144(1), p156-62; L.I.Liang et al, *Mercury reactions in the human mouth with dental amalgams*, Water, Air, and Soil pollution, 1995, 80:103-107. Sellars WA, et al, Univ. Of Texas Southwestern Medical School, *Methyl mercury in dental amalgams in the human mouth*, Journal of Nutritional & Environmental Medicine 1996; 6(1): 33-37; Yamada, T, *Formation of methyl Mercury Compounds from inorganic Mercury by Clostridium cochlearium*, J Ferment Technol 1972 50:159-1660; S. Yannai et al, *Transformations of inorganic mercury by candida albicans and Saccharomyces cerevisiae*, Applied Envir Microbiology, 1991, 7:245-247; Zorn NE, et al, *A relationship between Vit B-12, mercury uptake, and methylation*, Life Sci, 1990, 47(2):167-73; see also, <http://www.home.earthlink.net/~berniew1/amalg6.html> for many other cites to support this proposition.



actual dental procedures. Many mercury-using dentists are not skillful at placing composites which would make the training and experience of the dentists providing such services to the child-subjects relevant for the consent form. Such information is not included on the consent forms. This is yet another basis to conclude the consent forms are invalid.

The standard set out in Point 8 of The Code has not been met because the consent form did not include identification of all of the persons who would *conduct* or *engage* in the experiment. Without that information, a child-subject (or parent/guardian) is not able to determine whether all investigators or care providers are qualified or possess the necessary skill and care to the satisfaction of the subject.

**The Code, Point 9** states:

*During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.*

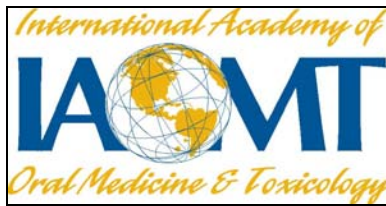
While the consent forms state that the subject is free to discontinue the study at any time, this is not always easy for children. The power disparity between adults and children makes any adult request inherently coercive. If the parents are economically disadvantaged, there may be undue pressure on the child to remain in the study for the perceived benefits of free dental care. If the child has no other source of spending money, the \$20 “surprise gift” (now \$50 – see analysis of child’s consent form below) may coerce the child into remaining in the study despite physical or mental discomfort. Truly, the child needs an independent advocate apart from the parents and the study team, who will ascertain the needs and desires of the child apart from the coercive elements of the study.<sup>86</sup>

**The Code, Point # 10** states that:

*During the course of the experiment the scientist-in-charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of good faith, superior skill and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.*

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<sup>86</sup> The CFRs contemplate the need for an independent advocate for the child-subject. 45 CFR 46.409 addresses the use of child-subjects who are wards of the State. If there is more than minimal risk inherent in the study (as there is here), then the regulation requires appointment of an advocate who has the background and experience to act in, and agrees to act in, the best interests of the child. <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm> (pages 31-32)



As set out in the comments to Point # 5 above, it was known prior to the experiment that the study was likely to result in injury, disability or possibly even premature death (mercury causes immune suppression which can be deadly for cancer patients).<sup>87</sup>

Apparently no preliminary results from the American portion of the study have been published or presented. However, On December 12, 2003, a PowerPoint presentation on the study was presented to the FDA/NIDCR mercury amalgam scientific panel being facilitated by Life Sciences Research Organization (LSRO). That presentation<sup>88</sup> indicates that on July 1, 2003, data was “frozen” for a DSMB report (Data and Safety Monitoring Board). Presumably, that review Board has found no reason to stop the study since Dr. Bellinger, who presented the slide presentation to the scientific panel, indicated that 48 month and 60 month outcomes are still pending.<sup>89</sup>

**However, preliminary results of the Casa Pia study reveal that the children’s urine mercury levels have risen extremely quickly to known harmful levels and those results should cause concern for the investigators of the American study as well. See pages 30-32. Is the DSMB aware of the Echeverria study showing adverse health effects at urine levels < 4 ug/l?<sup>90</sup>**

*(2) The Children’s Consent Form.* The consent form tells the child that he/she will receive fillings that are needed; that some children will get “shiny ones” and others

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<sup>87</sup> Mercury is a mutagen (harms the human germ cell which may lead to precancers). Schoeny R. *Use of genetic toxicology data in US EPA risk assessment: the mercury study report as an example*, Environ Health Perspect, 1996 May; 104 Supl 3:663-73; Low levels of mercury interfere with lymphocyte signaling leading to immune cellular dysfunction. Rosenspire, AJ, et al, *Low levels of ionic mercury modulate protein tyrosine phosphorylation in lymphocytes*, Int J Immunopharmacol 1998 Dec; 20(12):697-707; Low levels of body mercury equate to low levels of cancer. Foster, HD, *Landscapes of longevity: the calcium-selenium-mercury connection in cancer and heart disease*, Med Hypotheses 1997 Apr; 48(4):355-60; Male mercury miners have an increase in lung cancer and liver cancer and female workers have an excess of ovarian cancer. Bofetta P, et al, *Cancer occurrence among European mercury miners*, Cancer Causes Control, 1998 Dec; 9(6):591-9; Mercury has an influence on thyrocytes and plays a major role in thyroid cancer. Zaichick V Ye, et al, *Trace elements and thyroid cancer*, Analyst 1995 Mar; 120(3):817-21; Men occupationally exposed to mercury have an increased risk of brain cancer (gliomas). Navas-Acien, A, et al, *Occupation, exposure to chemicals and risk of gliomas and meningiomas in Sweden*, Sweden, Am J Ind Med 2002 Sep; 42(3):214-27 and Bjorklund, G, *Mercury in the dental office. Risk evaluation of the occupational environment in dental care*, Tidsskr Nor Laegeforen 1991 Mar 20; 111(8):948-51; Men and women fur hat workers occupationally exposed to mercury had significantly higher mortality from stomach cancer; there was a significant excess of lung cancer in women. Merler, E, *A cohort study of workers compensated for mercury intoxication following employment in the fur hat industry*, J Occup Med 1994 Nov; 36(11):1260-4; Mercury can induce granuloma which stimulates malignant melanoma. Kadykow, M, *Mercury-induced granuloma stimulating malignant melanoma*, Przegl Dermatol 1986 Mar-Apr; 73(2):147-51; and, 75-year-old male implanted with a mercury zinc pulsator under right breast developed breast cancer and the mercury was considered causative. Rasmussen, K, *Male breast cancer from pacemaker pocket*, Clin Electrophysiol 1985 Sep; 8(5):761-3.

<sup>88</sup> [http://www.lsro.org/presentation\\_files/amalgam/2003\\_12\\_12/bellinger.ppt](http://www.lsro.org/presentation_files/amalgam/2003_12_12/bellinger.ppt)

<sup>89</sup> *Id.*

<sup>90</sup> See footnote 24.



will get “white ones” and “right now, we don’t know which ones you will get. It will be a surprise.”<sup>91</sup>

The consent form tells the child that he/she will visit the dentist twice a year, have their teeth checked and cleaned, have treatments to prevent cavities, and have fillings placed if needed. It explains testing protocols. It promises the child “a present at the special visits” (for testing) but not on the regular dental visits. The consent form then asks: “Would you like us to explain which are the special visits when you will get a present?”

The consent form finally asks the child if they want to participate in the study and promises no one will be “mad” if the child says “no.”

First and foremost, a child does not have the legal capacity to give consent. That being said, 45 CFR 46.408 requires that an Institutional Review Board<sup>92</sup> solicit the assent of child-subjects when they are capable of assenting. Since this consent form attempts to obtain the assent of the child-subjects, the IRB must have determined that these children were capable of assenting. However, these children (and their parents) were not told that there is a controversy over the use of mercury-based dental fillings; that that controversy relates to the adverse health effects of the dental filling material; and, that an adverse outcome to the study will have an adverse economic impact on a large portion of practicing dentists.<sup>93</sup>

Children 8-10 years of age (the ages of the child-subjects at the outset of the study) are aware of the concept of “toxin” or “poison” as something to be afraid of, or at least concerned about. This consent form does not tell the children that there is toxic mercury in the dental fillings that can cause a wide array of health harm, nor does it disclose that there are cancer-causing chemicals in the composite fillings. It is a consent form without the information necessary for *informed consent*.

### **The Portuguese Consent Form.**

The Portuguese consent form includes a 7-page form for the parents or guardians and a separate 2 page consent form for the child-subjects.<sup>94</sup>

The children-subjects of this study are students at Casa Pia Schools in Lisbon, Portugal. The original school was founded in 1780 for “poor, orphans and helpless children.”<sup>95</sup>

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<sup>91</sup> Copies of the consent forms are available from [Barbara@toxicteeth.org](mailto:Barbara@toxicteeth.org) .

<sup>92</sup> The IRB is a review board charged with protecting human subjects from harm in National Institutes of Health research studies. <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm> Presumably the DSMB referred to in the American study is a form of IRB.

<sup>93</sup> Approximately 28% of practicing dentists are mercury-free according to the Utah-based Christiansen Research Institute.

<sup>94</sup> Copies are available from Consumers for Dental Choice [Barbara@toxicteeth.org](mailto:Barbara@toxicteeth.org) .

<sup>95</sup> <http://www.casapia.pt/ingles/History/history.html>



The schools now have 4600 children and include deaf, deaf mute, deaf and blind, children with other handicaps, orphans and day students.<sup>96</sup>

Lead investigator, Dr. Timothy DeRouen, speaking at a King County Board of Health (Seattle, WA) hearing on February 15, 2003, appeared as a member of a pro-amalgam panel. His presentation was on the ongoing Children's Amalgam Study and the preliminary results of the Casa Pia portion of the study. Dr. DeRouen indicated to the Board that there had been questions as to why they were using Portuguese children for this study. He explained that:

*We knew of the availability of these children to potentially participate in the study. The advantages of doing the study there include (PowerPoint slide):*

- (1) Extensive social network of contacts for each student enhances tracking.*
- (2) Relationship between University of Lisbon study personnel and Casa Pia already established.*
- (3) Cooperation and enthusiasm of the Casa Pia Schools administrators to facilitate study.*

Dr. DeRouen does not disclose that some of these children are in an institutional boarding school setting which includes orphaned and handicapped children. At least some of the children at Casa Pia are very disadvantaged and that raises serious concerns about their bargaining power to consent to participate in this study. The consent forms for parent/guardian and for the subject-child, are wholly inadequate and fail every requirement of the Nuremberg Code. These forms do not even contain the gloss of disclosure found in the American counterparts.

The federal regulations relating to American research subjects (45 CFR 46) also apply to research subjects in other countries if it is federally funded research. Thus, the regulations clearly apply to this study on behalf of the Portuguese children. The IRB Guidebook states:

*It is important that all research with human subjects adequately protect the rights and welfare of the subjects. All human subjects' research [outside of the U.S.] in which American investigators are involved, and which would be subject to the federal regulations if it were conducted wholly within the U. S., must comply with the federal regulations for the protection of human subjects in all material respects. Citing 45 CFR 46.001(h).*

(1) Parental Consent Form. Set forth below is an analysis of the parental form using the points from the Nuremberg Code and the CFRs.

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<sup>96</sup> *Id.*





**The Code, Point # 1:** (informed consent)

**The consent form does not inform the parents/guardians that amalgam dental fillings contain mercury.** It does not identify the brand or constituent components of the amalgam or the composite to be used. The information about the dental filling materials is limited to:

*There are two main types of tooth filling materials commonly used today. One is silver amalgam, and the other is a plastic composite material. Even though these filling materials are the standard ones used in hundreds of millions of fillings each year throughout the world, questions remain about the safety of the materials. We want to see if there is any ill effect of these materials on the health of children who have these materials placed in teeth for fillings.*

*To do this we will place one type or the other of filling material in the teeth that need fillings of each child who participate in the study. Both kinds of materials are normally used in the filling of teeth.*

The word “mercury” is only used once in this parental consent form on page 4. It indicates that a blood sample will be taken and tested to see how much mercury is in it. This reference to mercury does not inform a person that the proposed dental filling materials contain any mercury, let alone that they that they are 50% mercury.

The statements regarding the “risks, stress or discomfort” of the study are fraudulently misleading and wholly inadequate. The form states:

*None of these examinations, treatments or tests is experimental. They are all procedures that are commonly used throughout the world. The only risks or discomfort from these procedures are the ones usually associated with routine dental care or with routine medical examinations and tests.*

The form goes on to describe discomforts which can be expected from a dental cleaning, anesthesia injections, blood sample extractions, nerve function tests, written tests and dental xrays (the xray description does not identify the type of radiation, the amount in units of measurement or the risks of radiation exposure).

Despite the disclaimer to the contrary, this study *is* experimental. An “experiment” is defined as:

1. A test made to demonstrate a known truth, to examine the validity of a hypothesis, or to determine the efficacy of something previously untried. 2. The process of conducting a test. *The American Heritage Dictionary: Second College Edition*, Houghton Mifflin Company, Boston 1985.



The consent form itself admits that the purpose of the study is: “...to see if there is any ill effect of these [dental filling materials] on the health of children who have these materials placed in teeth for fillings.” (page 1) The “null hypothesis” of the study is that there will be no health differences demonstrated between the amalgam and composite groups. Testing the validity of that hypothesis is the goal of the study.<sup>97</sup>

The study researchers have asserted that it is unknown whether dental filling materials cause health harm and that this study is designed to determine the answer to that inquiry. This study is the classic example of an “experiment.”<sup>98</sup>

The fact that mercury amalgam has been used for over a hundred years (actually, over 170 years) on millions of people (the ADA’s “best defense for amalgams”) does not negate the fact that this study is an experiment. It is the first large, prospective, controlled study on the safety of dental material in a human population.<sup>99</sup>

Unlike the American parents’ consent form, this consent form does not even disclose the risks of acute exposure to mercury generally, or the known low level, chronic mercury exposure risks that have been identified in published studies.<sup>100</sup> There is a clear conflict of interest between the administrators of the school who will save the expenses of dental care for their wards. They could even have a personal pecuniary interest if these lower school expenses translate to wage increases for the administrators. The children must have a guardian/advocate whose sole interest is the child’s best interests – that did not occur here.

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<sup>97</sup> See, Dr. Tavares’ statement on the study hypothesis, footnote # 49.

<sup>98</sup> The FDA has never designated a risk classification for amalgam (a “dental device” within the jurisdiction of the FDA Dental Division) even though Congress passed a bill in 1976 that required it to do so. [FR 41(157)34099, 12 Aug 1976] Consumer advocates have taken actions to require FDA to classify amalgam as a Class III dental device (for which the manufacturer must prove efficacy and safety), but to date have been unsuccessful. In 2002 FDA took steps to classify amalgam as a Class II device (safe with labeling), but consumer advocates succeeded in convincing the FDA that a new scientific review panel needed to look at the published peer-reviewed scientific studies since the last review panel had been assembled in 1993. A scientific panel is now reviewing studies since 1996, however the panel is improperly constituted under the CFRs and its outcome is in the hands of pro-amalgamists at FDA and NIDCR.

<sup>99</sup> Since it is known that both amalgam and some composites contain toxic components, this is not really a controlled study which will show the harm from, or safety of, amalgams or the harm from, or safety of, composites, but rather the different effects of the two materials between the two groups. A true control group would have neither material, i.e. no fillings (or a known non-toxic filling material such as DiamondLite with a toxicity rating of “O” on the ADA/ANSI toxicity scale).

<http://www.biodent.com.au/biocompatibility.html>

<sup>100</sup> Echeverria, D. *Neurobehavioral effects from exposure to dental amalgam Hg(o): new distinctions between recent exposure and Hg body burden*, FASEB J. 1998 Aug;12(11):971-80 (presents convincing new evidence of adverse behavioral effects associated with low mercury exposures within the range of that received by the general population from mercury amalgams i.e. <4 ug/l.); [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9707169&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9707169&dopt=Abstract)



**And, of critical importance, the Casa Pia schools have been embroiled in a terrible scandal revealed in November of 2002 which alleged that many children were sexually abused by school employees who also provided criminal access to the children for politicians, media personalities, academics and others. International media have recently published articles (December 2003) disclosing the indictments of 10 high profile personages in Portugal for sexual abuse of an estimated 100 Casa Pia children.<sup>101</sup>**

**While the top administrator at the schools has been replaced, the former administration and other employees who worked at the schools at the time the Children's Amalgam Study began, were clearly failing to protect the Casa Pia school children and therefore, any consents which were executed for participation in this study are invalid for that reason alone.**

There is a normal, inherent inequality of power between a child and an adult. This is problematical in the American portion of the study when custodial parents were involved in giving consent for their children's participation in the study. But, the Portuguese study, if it involves orphans and handicapped children, who have been living in the milieu of sexual abuse extending back for decades, would place great pressure on these children to cooperate with their guardians' wishes or risk an unspeakable consequence.

Furthermore, it is inconceivable that the Portuguese research investigators at the University of Lisbon who have an ongoing relationship with the children, could have been ignorant of the abuse of these children at the outset of the study since the abuse was ongoing for three decades or more. The children's participation in any kind of clinical trials could never have been with valid consent. And certainly from the time of the public disclosure of the scandal in November 2002 to the Portuguese public, the investigators were on notice that their subjects were intimidated and powerless and their guardians could not give a valid consent because of conflicts of interest.

Between the lack of *any* informational disclosure concerning the risks of the dental materials involved, and the truly captive, abusive environment of the Casa Pia schools, all of the consents for all of these children are invalid and void *in abnatio*.

***The Code, Point ## 2-7:*** (these points relate to the likelihood of ascertaining worthwhile results unprocurable by other methods; to existence of animal studies justifying this study; to injury being avoided; to avoiding any risk which might exceed the human benefit expected) See the responses under the American consent form critique, above.

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<sup>101</sup> <http://www.sundayherald.com/37405> ;  
[www.couriermail.news.com.au/common/story\\_page/0,5936,8284156%255E1702,00.html](http://www.couriermail.news.com.au/common/story_page/0,5936,8284156%255E1702,00.html) ;  
<http://news.bbc.co.uk/1/hi/world/europe/3086521.stm>  
[www.charleston.net/stories/123103/wor\\_31portugal.shtml](http://www.charleston.net/stories/123103/wor_31portugal.shtml)



**The Code, Point # 8:** (scientifically qualified persons conducting the studies)

The principal investigator is Timothy A. DeRouen, PhD, Professor and Chair of the Dental Public Health Sciences, University of Washington. Several years ago Dr. DeRouen told the Development Director for Consumers for Dental Choice<sup>102</sup> that he knew “next to nothing” about mercury toxicity from amalgams and “frankly [do not] want to know.”<sup>103</sup> This is a rather amazing statement in light of the responsibilities of the investigators in human clinical trials. The last paragraph of Point # 1 of The Code, relating to voluntary consent states:

*The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.*

It is clear that Dr. DeRouen, the principle investigator for the Casa Pia school children branch of the Children’s Amalgam Study, could not obtain informed consents from subjects when he himself is uninformed about the risks of mercury amalgam. He obviously delegated that duty to some administrator (but not the responsibility) in violation of The Code.

J. Thomas Puglisi, PhD, the Director of the Division of Human Subject Protections, Office for Protection from Research Risks (OPRR),<sup>104</sup> in a memo dated January 26, 1999, reminded his Division that research institutions involved in research with human subjects must provide Assurances as required by 45 CFR 46, *et seq.*, and declared: “...the awardee institution bears ultimate responsibility for protecting human subjects under the award.”<sup>105</sup> The University of Washington and the University of Lisbon are the responsible institutions for the Casa Pia portion of the study and they have failed to protect their child-subjects.

Dr. DeRouen is listed as an author on 97 studies in the PubMed database. Many of these articles relate to periodontitis and a possible link to systemic disease – mostly bacteria related. He has no published studies related to mercury or amalgam except preliminary articles related to the Children’s Amalgam Study.<sup>106</sup>

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<sup>102</sup> Freya Koss, Wynnewood PA, is the Development Director for Consumers for Dental Choice, a private non-profit which educates the public about the hazards of mercury amalgam dental fillings.

<sup>103</sup> *Personal communication with Freya Koss, Development Director for Consumers for Dental Choice, December 13, 2003.*

<sup>104</sup> Dr. Puglisi is no longer the Director. Bernard A. Schwetz is the Acting Director. The name of the office is now: Office for Human Research Protections; Department of Health and Human Services, The Tower Building, 1101 Wootton Parkway, Suite 200, Rockville, MD, 20852.

<sup>105</sup> <http://ohrp.osophs.dhhs.gov/humansubjects/assurance/engage.htm>

<sup>106</sup> <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=PubMed> (keyword “DeRouen T”).



Disclosed co-investigators of the Casa Pia school children branch of the Children's Amalgam Study include:

Michael D. Martin, DMD, MPH, PhD, Department of Oral Medicine, University of Washington. A search of PubMed revealed 53 articles listing MD Martin as an author. Based on the subject matter of some of these studies, some of the articles may not be authored by this investigator. Dr. Martin has done research related to mercury amalgam including a study that revealed that chronic low levels of mercury exposure from amalgams affected the hand steadiness of dentists.<sup>107</sup>

James Woods, toxicologist, in a conversation with Charles G. Brown, legal counsel for Consumers for Dental Choice, Washington D.C., in 2003, admitted that he is not actively involved in the Children's Amalgam Study. He said he was "window dressing" and stated he was "kept in the dark" regarding the study. Dr. Woods is listed as an author on 107 articles in the PubMed database. A number of the studies deal with the toxicity of mercury and the measurement of mercury body burden. A recent study that Dr. Woods authored, assayed the urine of inner city, mostly minority children, for mercury and concluded that 5% of these children had in excess of 5 ug/l in their urine. The study concluded that there needed to be an investigation of the source of this mercury overload.<sup>108</sup> Thus, Dr. Woods appears to be most qualified to be an investigator in this case and the failure of the other investigators to have him actively involved raises a concern that they are not truly interested in determining how much mercury the child-subjects are being exposed to, the source of the exposure and the results of the exposure.

Dr. Jorge Leitao, Coordinator in Portugal, Professor of Biomaterials, Faculty of Dental Medicine, University of Lisbon, Portugal. A search of the PubMed database shows 82 articles authored by "Leitao J," although some seem far afield of dental or mercury related matters.

Dr. A. Castro-Caldas, Director of Neurological Services and Professor at the Faculty of Medicine, University of Lisbon. A search of PubMed database shows 46 articles authored by "Castro-Caldas A." Dr. Castro-Caldas is the lead medical investigator in Portugal for the Casa Pia school children and should have the most knowledge related to the coercive and abusive environment these children were living in, and their incapacity to give informed consent.

There are, additionally, authors on published articles relating to the Children's Amalgam Study, who are *not identified* on the consent forms as investigators. Their roles are

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<sup>107</sup> Bittner, AC, et al, *Behavioral effects of low-level exposure to Hg0 among dental professionals: a cross-study evaluation of psychomotor effects*, Neurotoxicol Teratol. 1998 Jul-Aug;20(4):429-39.

<sup>108</sup> Ozuah P.O., et al, *Mercury exposure in an urban pediatric population*, Ambul Pediatr. 2003 Jan-Feb;3(1):24-6 (New York state).



unclear. One article is on the study design for the study: *Issues in design and analysis of randomized clinical trial to assess the safety of dental amalgam restorations in children.*<sup>109</sup> The authors include T. DeRouen, MD Martin, JS Woods, J Leitao, and A. Castro-Caldas who are identified as investigators in the consent form. Other listed authors include: BG Leroux, BD Townes and N. Braveman who are not listed on the consent form.

BG Leroux is listed in the PubMed database as an author in 35 studies. His study subjects include smoking and dental issues (not including mercury toxicity). One of the studies was conducted on 150 Portuguese children (the abstract does not identify them as Casa Pia school children) and related to candida of the mouth.<sup>110</sup>

BD Townes has 50 studies in the PubMed data base, most of which appear to be related to neuropsychology. Townes is listed as an author on a preliminary oral report on the Casa Pia study results which was reported to the International Association of Dental Research meeting in San Diego, CA March 6-9, 2002. These results have not been published, or at least are not in the PubMed data base.

Carina C. Evens, MS, PhD, Department of Dental Public Health Sciences is the lead author in a study of methylmercury in the Casa Pia children as part of the Children's Amalgam Study.<sup>111</sup> Evens is listed as an author in 3 other articles on the PubMed database. Two of them relate to mental health and one to lung cancer.<sup>112</sup>

Norman S. Braveman, DDS, Assistant to the Director at NIDCR, is a named author on articles that has been published related to the Children's Amalgam Study.<sup>113</sup> PubMed data base reveals 7 studies by N. Braveman. One relates to research infrastructure for Hispanic children.<sup>114</sup> Another related blood lead levels to incidence of caries in the New England children enrolled in the Children's Amalgam Study.<sup>115</sup> Four of the studies listed in PubMed relate to behavioral and psychological studies that are decades old; they

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<sup>109</sup> Control Clin Trials, 2002 Jun;23(3):301-20.

<sup>110</sup> Starr JR, et al., *Persistence of oral Candida albicans carriage in healthy Portuguese schoolchildren followed for 3 years*, Oral Microbiol Immunol. 2002 Oct;17(5):304-10.

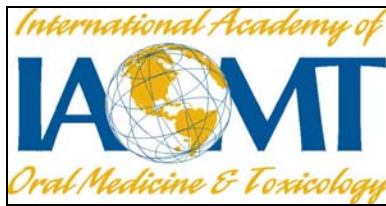
<sup>111</sup> Evens CC, et al, *Examination of dietary methylmercury exposure in the Casa Pia Study of the health effects of dental amalgams in children*, J Toxicol Environ Health A. 2001 Dec 7;64(7):521-30.

<sup>112</sup> Contact information for Dr. Evens: Box 357475, University of Washington, Seattle, WA 98195-7475, [cevens@u.washington.edu](mailto:cevens@u.washington.edu)

<sup>113</sup> DeRouen, T, et al, *Issues in design and analysis of a randomized clinical trial to assess the safety of dental amalgam restorations in children*, Control Clin Trials, 2002, June;23(3):301-320; and Evens, CC, et al, *Examination of dietary methylmercury exposure in the Casa Pia study of the health effects of dental amalgams in children*, J Toxicol Environ Health A 2001, Dec 7; 64(7):521-30.

<sup>114</sup> Braveman N, *Building an effective research infrastructure to meet the oral health needs of the Hispanic community*, Compend Contin Educ Dent. 2002 Dec;23(12 Suppl):46-7.

<sup>115</sup> Gemmel A, *Blood lead level and dental caries in school-age children*, Environ Health Perspect. 2002 Oct;110(10):A625-30.



probably are not the same person. It appears that Dr. Braveman lacks any substantial research credentials or research specific to mercury toxicity.

NIDCR will have awarded \$11 million in grants for The Children's Amalgam Study by the time it is completed.<sup>116</sup> It appears Dr. Braveman is not involved in the actual research project. The ethics of Dr. Braveman appearing to award himself a research grant is questionable. And, if he is not actually involved in the research, it is also ethically questionable whether he should be able to personally benefit from these grant awards by being able to pad his resume with these academic and publication credits.

Dr. Braveman is an apologist for mercury amalgam.<sup>117</sup> He is presently in charge of the contract for an "independent scientific review" of recent peer-reviewed literature on amalgam safety. This public contract was awarded in secret without a bid by tagging it to an ongoing FDA/NIDCR contract. Consumers for Dental Choice have spent almost a year filing FOIA requests related to these contracts that have been resisted by the FDA and the NIDCR.

The scientific panel members were chosen through a secret process. It specifically excluded researchers researching mercury or amalgam whose studies have concluded that there are health risks from amalgam. None of the panelists were aware of the amalgam controversy before becoming panelists and have been spoon-fed limited information by the pro-amalgam NIDCR and FDA Dental Devices Division.

With the exception of an 80-minute public hearing on December 12, 2003, all other sessions have been conducted in secret in violation of the Federal Advisory Committee Act.<sup>118</sup> The presenters at these sessions are vetted and invited based on the acceptability of their point of view. The stated goal of conducting this procedurally flawed scientific review is to conclude that the Children's Amalgam Study will answer the question of amalgam safety "once and for all" and that the scientific panel should just await the final published report on that trial. Meanwhile, the panel will conclude, as every other dental-interest-controlled "scientific panel" has concluded, that there is not conclusive proof

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<sup>116</sup> Statement of Michael D. Martin at the hearing before the King County Board of Health (Seattle, WA), February 15, 2003, tape available from KCCTV.

<sup>117</sup> Braveman was a member of the Working Group on Dental Amalgam that prepared a report to the Environmental Health Policy Committee of USDHHS in 1993. <http://web.health.gov/environment/amalgam2/Contents.html> The report dismissed all scientific studies implicating amalgam as a health risk and encouraged the continued use of mercury amalgam. One of the referenced works supporting the Working Group conclusions was Braveman's: *Research on the use and safety of dental amalgam: an overview and research agenda*. (Not available on the internet.) The question that needs to be asked is: did Braveman's report rely on the 500+ studies on amalgam funded by the NIDCR (since 1972) which have never been published? Braveman has a great deal of power to determine which NIDCR research projects are funded. Studies that could definitively answer the question of amalgam safety (comparing the health of subjects who have never had amalgams with those who have had 8-10 amalgams, the average for the American population) are never funded.

<sup>118</sup> 5 USC Appx Sections 1-15.



from “valid” studies (ones the dental industry agrees with) that amalgam causes any specific disease and dentists should continue to use it with confidence.<sup>119</sup>

A preliminary report on the Casa Pia study results was reported to the International Association of Dental Research meeting in San Diego, CA, March 6-9, 2002. The results have not been published, or at least are not in the PubMed data base. The authors listed in the convention materials as authors also include M. Bernardo, H. Soares and L. Simmonds.

Drs. Martin and Woods are the only researchers with expertise in mercury research, and Dr. Woods asserted he is being “kept in the dark.” The other disclosed and undisclosed investigators are working to prove the “null hypothesis” that amalgam does not cause health harm. This study is not blind because the child-subjects with amalgam are obvious. None of the names of the treating dentists have been disclosed.

It is expected that the FDA/NIDCR mercury amalgam scientific panel will conclude that none of the evidence before it conclusively proves that amalgam causes health harm and will recommend that the federal agencies await the Children’s Amalgam Study outcome.

The FDA Dental Devices Division and NIDCR are dedicated to protecting the *status quo* for the dental industry and to the perpetuation of amalgam usage.<sup>120</sup>

***The Code, Point # 9*** (subject may end experiment)\

It is unthinkable that the Casa Pia school children could be perceived to have any power to stop their participation in the amalgam study. This would be disadvantageous to the schools and, in light of the schools’ history of abuse, would be likely to trigger more abuse. The guardian consents were void *in abnatio*. The experiment must stop immediately.

***The Code, Point # 10*** (terminate experiment if adverse results)

Even assuming the consent was valid, the experiment must stop based on published studies showing that amalgam is likely to cause adverse health effects (as set out above).

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<sup>119</sup> But see, <http://www.testfoundation.org/vimyresponds.htm>, a document that lists peer-reviewed scientific articles that show that amalgam causes gingivitis and periodontal disease that has, in turn, been linked to heart disease, diabetes, low birth weight and pre-term birth.  
<http://www.calgaryhealthregion.ca/hecomm/oral/healthy.htm>.  
<http://www.altcorp.com/AffinityLaboratory/lbwinfants.htm>

<sup>120</sup> The dental industry has an economic interest in amalgam. For the manufacturers, it is an obvious commercial interest. For the dentists, there is an interest in the investment they have made in their education and in their professional experience. Additionally, dentists have a concern about the potential liability for harm to their patients, as well as loss of reputation as a health care provider. See, *In re Cincinnati Radiation Litigation*, 874 F. Supp. 796 (S.D. Ohio 1995).





There have been at least two presentations on the preliminary results reported by Dr. De Rouen on the Casa Pia arm of the Children's Amalgam Study, and those results give a reason for concern for the child-subjects because they show increasing urine mercury levels.

On February 15, 2003, Dr. DeRouen testified before the King County Board of Health (Seattle, WA), that the average mercury urine level after **three years** was at 3.2 ug/l, from a baseline of 1.4-1.5 ug/l. Dr. DeRouen characterized that change as "insignificant" and "within a background level." In fact, it represents **more than a 100% increase in 3 years** with another 2-4 years<sup>121</sup> to go to completion of the study.<sup>122</sup>

Almost a year earlier (March 6-9, 2002) the preliminary results of the Children's Amalgam Study were presented by Dr. DeRouen at the International Association of Dental Research (IADR) in San Diego, CA, and the statistics were even grimmer. The abstract on the IADR website did not cite the baseline urine mercury levels which were reported at the conference. It did, however, set out the annual urine mercury measurements which were reported by DeRouen at the conference. Those results were as follows:

At **one year** after placement of restorations, the amalgam group results were: 2.49 ug/l, while the composite group was: 1.29 ug/l. It is puzzling that the composite group one-year results were lower than the baseline figures reported to the King County Board of Health.

At **two years** after placement, the amalgam group results were: 3.24 ug/l, while the composite group was: 1.52 ug/l. (Note: This result for urine mercury level is higher than the **three year** results reported to the King County Board of Health.)

At **three years** after placement, the amalgam group results were: 4.22 ug/l, while the composite group was: 1.82 ug/l. **This is a 300% increase in urine mercury in the children with amalgam fillings!** Eleven months later Dr. DeRouen reported the three year results to the King County Board of Health as 3.2 ug/l for children with amalgams and 1.8 for children with composites. Dr. DeRouen either misspoke or intentionally mislead the King County Board of Health in Seattle.

Also significant are Casa Pia statistics which show that children who only had the initial amalgam fillings, with no additional fillings placed in the first two years, had a mean HgU of 2.52 ug/l, while those who had additional amalgam fillings placed in the first two years had a mean HgU of 4.26 ug/l. Even if the baseline mercury level was the 1.4-1.5

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<sup>121</sup> The Children's Amalgam Study has been variously described as a 5-year and a 7-year study.

<sup>122</sup> King County Cable TV, February 15, 2003. Video tape of the Board meeting is available from KCCTV.



reported to the King County Board of Health, there was almost a doubling of urine mercury for those with only the initial amalgam fillings.<sup>123</sup>

Dr. DeRouen described the urine mercury increase to the King County Board of Health as insignificant ignoring studies that show that < 4 ug/l can cause measurable impairments.<sup>124</sup> According to the information presented to the IADR conference, the children with amalgam exceeded that 4 ug/l level prior to March of 2002. It is now two years later. It is almost certain that urine mercury levels have risen even higher.

And, these researchers are ignoring the fact that in susceptible subjects, any level of mercury can trigger autoimmune disease.<sup>125</sup> While there has not been any public disclosure of urine mercury levels of the American children, it is reasonable to believe that they are also bioaccumulating mercury in their bodies on account of their amalgams.

A peer-reviewed study by *Holmes, et al*, that was recently published shows that children with the lowest mercury excretion levels (as shown by urine, blood and hair levels) are likely to be retaining the most mercury.<sup>126</sup> Has the research team made appropriate adjustments to its protocols to identify subjects who may be poor excretors and therefore presumably accumulating high levels of mercury? At a minimum, those children should be removed from the study for the protection of their health.

The *Holmes* study completely undermines the dose-response assumptions (the dose makes the poison) underlying the Children's Amalgam Study. As noted previously, Kazantzis, in his peer-reviewed survey article concludes that if, as is evident in many reviewed studies, very low levels of mercury can trigger autoimmune responses in susceptible persons, then there is no safe level of mercury exposure.<sup>127</sup>

The failure of the Children's Amalgam Study to make any attempt to identify susceptible dental consumers who should not be exposed to mercury, is grounds for immediately

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<sup>123</sup> [http://iadr.confex.com/iadr/2002SanDiego/techprogram/abstract\\_20128.htm](http://iadr.confex.com/iadr/2002SanDiego/techprogram/abstract_20128.htm)

<sup>124</sup> Echeverria, D. *Neurobehavioral effects from exposure to dental amalgam Hg(o): new distinctions between recent exposure and Hg body burden*, FASEB J. 1998 Aug;12(11):971-80 (presents convincing new evidence of adverse behavioral effects associated with low mercury exposures within the range of that received by the general population from mercury amalgams i.e. <4 ug/l.); [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9707169&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9707169&dopt=Abstract)

<sup>125</sup> Kazantzis, G., *Mercury exposure and early effects: an overview*, Med Lav. 2002 May-Jun;93(3):139-47.

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=12197264&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12197264&dopt=Abstract)

<sup>126</sup> Holmes, AS, et al, *Reduced levels of mercury in first baby haircuts of autistic children*, Int J Toxicol, 2003 Jul-Aug; 22(4):277-85.

<sup>127</sup> See footnote # 65.



stopping this study to protect this most vulnerable population (poor excretors) which, statistically, would include children in the subject population.<sup>128</sup>

Also, see Point # 10 for the American consents, above.

### (2) Children's Consent Forms.

The children's consent form is also wholly inadequate. It does not tell the children that toxic mercury is being placed in their teeth, or that toxic composites are the other possibility. The only mention of mercury in this consent form is in a description of the study that states:

*We want to know if there is mercury or lead in your body in normal quantities.*

This reference to mercury would not inform a person that the proposed dental filling materials contain any mercury let alone that they are 50% elemental mercury (the fillings do not contain lead, but the investigators are testing lead levels). The risks identified are only those discomforts which are associated with dental exams, obtaining urine samples and blood samples, nerve conduction tests and a written exam.

Even assuming these children had the capacity for consent, since these children are Portuguese, presumably their first language is Portuguese. There would be a question as to whether or not a proper translation of the consent form was made for these children. And, for the children who are deaf, blind or otherwise handicapped, there would be a question of proper communication of the information contained in the consent form, as well as the child's comprehension of what it means.<sup>129</sup>

All of the comments to the Nuremberg Code points set out above apply here as well.

### **Case law on clinical trial liability.**

All it will take for this clinical trial to end up in a courtroom is for a trial lawyer to connect the following dots: (1) The consent forms used in this study violate federal regulations, the Nuremberg Code and common law; (2) The children with amalgam fillings (at least in the Casa Pia portion of the study) now have mercury levels that have

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<sup>128</sup> Maths Berlin, PhD, WHO expert, and Professor Emeritus of Environmental Medicine in Sweden, has reported that 1-10% of the population is especially vulnerable to an autoimmune response to mercury in amalgams; in the US this equates to 3-30 million susceptible people; in the Children's Amalgam Study this equates to 10-100 susceptible child-subjects.

[http://www.social.regeringen.se/propositionermm/sou/pdf/2003/sou2003\\_53eng.pdf](http://www.social.regeringen.se/propositionermm/sou/pdf/2003/sou2003_53eng.pdf)

<sup>129</sup> The IRB Guidebook requires that subjects who speak a foreign language be given consent forms in their native language and speak to competent interpreters. *IRB Guidebook, Chapter 6ii, special classes of subjects, pp 11-12.*



been demonstrated to cause neurological damage, i.e. > 4 ug/l; and (3) The children's damages include any actual harm (what is the value of 5 IQ points or impaired kidney function?), costs to remove and replace the mercury amalgam fillings, medical treatments to remove mercury from the body (chelation and other detoxification), medical treatments for any mercury induced diseases or other harm, and lifelong medical monitoring.

Parents and guardians can sue for harm to their children. A group of child-subjects can commence a class action.

While the investigators might defend with an assertion that the treatment for the children meets the standard of care in the community for dental care, this might be the perfect forum in which to assert that the standard of care in the dental community (using mercury as a dental filling material) is a negligent standard of care. Mercury amalgam dental fillings have never been proven safe by manufacturers (even though the ADA has given them its "Seal of Acceptance"). And, the FDA has never classified mercury amalgams, which impliedly, would constitute an agency approval of the dental devices. Of course, even an appropriate standard of care is not a defense for failure to obtain informed consent.

Logically, manufacturers of amalgam should be able to be held liable for harm to dental consumers from their products, however, if they provided adequate warnings to dentists, the "Learned Intermediary" doctrine might insulate them from liability.<sup>130</sup> That doctrine places a heavy burden on health care providers who are in a "special relationship" with their patients. Patients reasonably rely on dentists to know all relevant facts about the dental devices dentists use. (ADA Ethics Rule # 5 D, advisory opinion 5 D 2, imposes on dentists an independent obligation to: "... Inquire into the truth and accuracy of ...claims [of a product's safety and efficacy] and verify that they are founded on accepted scientific knowledge or research.") The investigators and dentist-providers in the Children's Amalgam Study have a duty to warn the dental consumer of material hazards, complications, foreseeable risks, reasonable alternatives, effects of non-treatment and the lack of necessity for treatment.

If dentists intentionally or negligently fail to apprise themselves of the facts about the safety and efficacy of dental devices, they will be held liable for adverse outcomes. Dentists treating the child-subjects have a duty to advise of any financial interest they may have in the clinical trial. Here, the dentists have an economic interest in the continuation of the use of amalgam; this was not disclosed.

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<sup>130</sup> See, *Kernke v. Menninger Clinic*, 173 F. supp. 1117 (D. Kan. 2001) (research subject died after being given experimental drug for schizophrenia and her relatives sued the pharmaceutical company and the clinic conducting the trial, claiming that the informed consent form was flawed. The court dismissed the pharmaceutical company, absolving it under the "learned intermediary doctrine," because it had given relevant safety and efficacy information to the clinic in the drug brochure, any liability would lie with the clinic, not the pharmaceutical company).



There have been a number of lawsuits relating to human experiments which indicate that investigators and members of Institutional Review Boards (IRBs) have potential liability. Several of them are set forth below:

In *Diaz v. Hillsborough County Hospital Authority*<sup>131</sup> 380 women sued Tampa General Hospital for performing medical experiments on them including multiple amnios when they were pregnant, allegedly without their consent. The court approved a settlement (\$3.8 million) of a class action lawsuit (3200 plaintiffs) for “dignitary harm resulting from the violation of the plaintiffs’ liberty interest in bodily integrity in the absence of any claim of physical harm.” The child-subjects of the Children’s Amalgam Study may be able to claim and prove actual harm.

In *Robertson v. McGee*,<sup>132</sup> plaintiffs were in a clinical trial for vaccine treatment of melanoma. Plaintiffs alleged lack of informed consent because the defendants failed to follow federal human subject regulations (45 CFR 46, *et seq.*). The defendants were the Oklahoma University School of Medicine, the University administration and individual IRB members. The court held that a 42 USC Section 1983 action could not be based on failure to follow federal regulations because there is no private right of action under 45 CFR 46 and therefore, no federal claim had been alleged.<sup>133</sup> There was a partial settlement of the case which included the IRB members.

If plaintiffs in *Robertson* had alleged that vaccine injections without informed consent was a violation of the plaintiffs’ fundamental federal constitutional right to bodily integrity, a federal claim would have been alleged.<sup>134</sup> The state action requirement is satisfied in the Children’s Amalgam Study because one of the investigation institutions is a public university (University of Washington), and both arms of the study include Norman Braveman of the National Institute of Dental and Craniofacial Research Institute as an investigator. The participation of Dr. Braveman in conjunction with New England Research Institutes (NERI - a private entity involved in the American branch of the study), as well as the NIDCR financing of the study, shows that NERI was jointly engaged with government officials, satisfying the state action requirement, a basis for a Section 1983 action.<sup>135</sup>

The *Robertson* case was cited in the Journal of Law, Medicine and Ethics, in an article about the potential liability of members of an Institutional Review Board. The article states:

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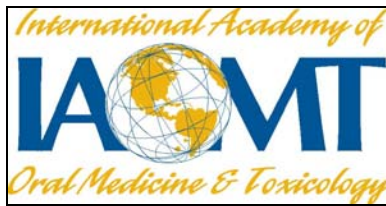
<sup>131</sup> 165 FRD 689 (MD Fla. 1996).

<sup>132</sup> Case No. 01-CV-60-C; 2002 U.S. Dist. LEXIS 4072 (January 28, 2002).

<sup>133</sup> See, *Grimes v. Kennedy Krieger Institute*, 782 A2d 807 (Court of Appeals MD 2001) (where the court accepted the regulations in 45 CFR 46 *et seq.* as a standard for negligence).

<sup>134</sup> *In Re Cincinnati Radiation Litigation*, 874 F. Supp. 796 (S.D. Ohio 1995).

<sup>135</sup> *Id.*



*Despite the recognition that too much responsibility has been laid upon them, IRB members – both individually and as a board – may be exposed to legal liability for any failures, deliberate or otherwise, associated with the human subjects research they are charged with approving and monitoring. The Robertson case illustrates this danger.<sup>136</sup>*

The *Wright*<sup>137</sup> case in Washington State was scheduled to go to trial in February 2004. It arose out of the death of a bone marrow transplant subject at Fred Hutchinson Cancer Research Center. The causes of action included: right to be treated with dignity; FDA regulations non-compliance; Belmont Report ethical violations; fraud/intentional misrepresentation; assault and battery; strict product liability; and, state consumer protection law violations. The factual issues at trial will determine if the defendants knew of prior adverse reactions and failed to warn or test; if there was deceptive advertising and promotion; whether defendants concealed information from government regulators; and, if investigators had financial interests. That this case *is* actually going to trial means that the many hurdles to get there (jurisdiction, stating a cognizable claim, etc.) have been overcome.

*Gelsinger v. University of Pennsylvania*<sup>138</sup> is another case involving an inadequate consent form. The 18 year-old subject had a rare metabolic disorder and entered a gene transfer clinical trial. The consent form did not reveal that there had been deaths of monkeys used in pre-trial animal studies; that there had been previous adverse events; and, did not reveal a monetary relationship between the principal investigator and the University of Pennsylvania. After an injection of adenovirus vector, the subject died. A confidential settlement was reached between the plaintiffs and the University.

The lawsuit which gives the greatest guidance in an analysis of liability in the Children's Amalgam Study is: *Grimes v. Kennedy Krieger Institute*.<sup>139</sup> In this case, a research institute failed to adequately warn child-subjects of lead exposure in a non-therapeutic scientific study and the children had alarming increases in blood-lead levels during the pendency of the study. The facts as stated by the court are:

*In these present cases, a prestigious research institute, associated with Johns Hopkins University ... created a nontherapeutic research program whereby it required certain classes of homes to have only partial lead paint abatement modifications performed, and in at least some instances, including at least one of the cases at bar, arranged for the landlords to receive public funding by way of grants or loans to aid in the modifications. The research institute then*

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<sup>136</sup> Anderlik, Mary R, et al, *Currents in contemporary ethics*, Journal of Law, Medicine & Ethics, Summer, 2001. [http://www.findarticles.com/cf\\_dls/m0DPE/2\\_29/77355600/p1/article.jhtml?term=](http://www.findarticles.com/cf_dls/m0DPE/2_29/77355600/p1/article.jhtml?term=)

<sup>137</sup> Kitsap County Superior Court, WA (March 2001). CAUSE NO.: 01-2-008376.

<sup>138</sup> C.P. Phila. Co., 2000, <http://www.sskrplaw.com/gene/gelsinger.html>

<sup>139</sup> 782 A.2d 807 (Ct. of Appeals, MD 2001).

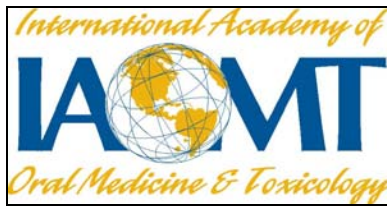


*encouraged, and in at least one of the cases at bar, required, the landlords to rent the premises to families with young children. In the event young children already resided in one of the study houses, it was contemplated that a child would remain in the premises, and the child was encouraged to remain, in order for his or her blood to be periodically analyzed. In other words, the continuing presence of the children that were the subjects of the study was required in order for the study to be complete. Apparently, the children and their parents involved in the cases sub judice were from a lower economic strata and were, at least in one case, minorities. At 812.*

*The same researchers had completed a prior study on abatement and partial abatement methods that indicated that lead dust remained and/or returned to abated houses over a period of time. In an article reporting on that study, the very same researchers said: "Exposure to lead-bearing dust is particularly hazardous for children because hand-to-mouth activity is recognized as a major route of entry of lead into the body and because absorption of lead is inversely related to particule size." Mark R. Farfel & J. Julian Chisolm, *Health and Environmental Outcomes of Traditional and Modified Practices for Abatement of Residential Lead-Based Paint*, 80 American Journal of Public Health 1240, 1243 (1990). After publishing this report, the researchers began the present research project in which children were encouraged to reside in households where the possibility of lead dust was known to the researcher to be likely, so that the lead dust content of their blood could be compared with the level of lead dust in the houses at periodic intervals over a two-year period. *Id.**

*Apparently, it was anticipated that the children, who were the human subjects in the program, would, or at least might, accumulate lead in their blood from the dust, thus helping the researchers to determine the extent to which the various partial abatement methods worked. There was no complete and clear explanation in the consent agreements signed by the parents of the children that the research to be conducted was designed, at least in significant part, to measure the success of the abatement procedures by measuring the extent to which the children's blood was being contaminated. It can be argued that the researchers intended that the children be the canaries in the mines but never clearly told the parents. (It was a practice in earlier years, and perhaps even now, for subsurface miners to rely on canaries to determine whether dangerous levels of toxic gasses were accumulating in the mines. Canaries were particularly susceptible to such gasses. When the canaries began to die, the miners knew that dangerous levels of gasses were accumulating.) At 812-813.*

*The researchers and their Institutional Review Board apparently saw nothing wrong with the search protocols that anticipated the possible accumulation of lead in the blood of otherwise healthy children as a result of the experiment, or they believed that the consents of the parents of the children made the research*



appropriate. Institutional Review Boards (IRB) are oversight entities within the institutional family to which an entity conducting research belongs. In research experiments, an IRB can be required in some instances by either federal or state regulation, or sometimes by the conditions attached to governmental grants that are used to fund research projects. Generally, their primary functions are to assess the protocols of the project to determine whether the project itself is appropriate, whether the consent procedures are adequate, whether the methods to be employed meet proper standards, whether reporting requirements are sufficient, and the assessment of various other aspects of a research project. One of the most important objectives of such review is the review of the potential safety and the health hazard impact of a research project on the human subjects of the experiment, especially on vulnerable subjects such as children. Their function is not to help researchers seek funding for research projects. At 813. (Emphasis added.)

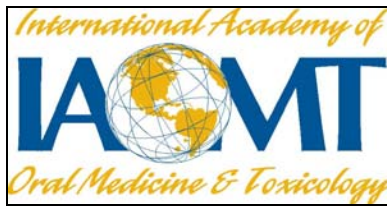
The court's recitation of the facts does not disguise its outrage with the entire scientific study. Many of the facts in *Grimes* are analogous to the Children's Amalgam Study. In *Grimes*, the child-subjects were purposefully exposed to neurotoxic lead while the child-subjects in the Children's Amalgam Study are being purposefully exposed to mercury, which is toxic to neurons, enzymes, proteins and hormones. In *Grimes* the child-subjects were poor and mostly minority, as are the child subjects in the Children's Amalgam Study.

In *Grimes* the child-subjects were not receiving any potentially therapeutic treatment. Certainly the investigators in the Children's Amalgam Study will claim that the child-subjects were receiving therapeutic standard dental care for free, which distinguishes this matter from *Grimes*. However, it is also "standard" for poor children to be regularly exposed to lead paint in old housing, yet the court found it was unethical, immoral and illegal for the researchers to design a study to purposefully expose children to a known harmful toxin – lead. Similarly, while it may be "standard" for poor children to receive mercury amalgam dental fillings, it is unethical, immoral and illegal to design a study to expose children to a toxin known to be 40 times more toxic than lead, which is expected to accumulate in their bodies and is known to cause health harm. The primary purpose of the Children's Amalgam Study is to protect the economic interests of the dental industry which means that the experiment, like *Grimes*, is not therapeutic.

The *Grimes* case was before the Court of Appeals because the trial court had granted defendants Motion for Summary Judgment which meant that the defendants won a dismissal as a matter of law. The Court of Appeals, however, found that there were factual issues to be determined by a jury and stated:

*We hold that in Maryland a parent, appropriate relative, or other applicable surrogate, cannot consent to the participation of a child or other person under*





*legal disability in nontherapeutic research or studies in which there is any risk of injury or damage to the health of the subject....*

*We hold that informed consent agreements in nontherapeutic research projects, under certain circumstances can constitute contracts; and that, under certain circumstances, such research agreements can, as a matter of law, constitute “special relationships” giving rise to duties, out of the breach of which negligence actions may arise. We also hold that, normally, such special relationships are created between researchers and the human subjects used by the researchers. Additionally, we hold that governmental regulations can create duties on the part of researchers towards human subjects out of which “special relationships” can arise. Likewise, such duties and relationships are consistent with the provisions of the Nuremberg Code.*

*The determination as to whether a “special relationship” actually exists is to be done on a case by case basis. (cite omitted) The determination as to whether a special relationship exists, if properly pled, lies with the trier of fact. We hold that there was ample evidence in the cases at bar to support a fact finder’s determination of the existence of duties arising out of contract, or out of a special relationship, or out of regulations and codes, or out of all of them, in each of the cases.*

*We hold that on the present record, the Circuit Courts erred in their assessment of the law and of the facts as pled in granting KKI’s motions for summary judgment in both cases before this Court. At 858.*

The court recognized the principles set out in The Nuremberg Code and found that there were violations of The Code which set standards and could be the basis of a claim. The court stated:

*The Constitution’s promise of due process of law guarantees at least compensation for violations of the principle stated by the Nuremberg Military Tribunals that the voluntary consent of the human subject is absolutely essential to satisfy moral, ethical and legal concepts ...At 817.*

*The Nuremberg Code requires that the informed, voluntary, competent, and understanding consent of the research subjects be obtained. Although this principle is placed first in the code’s 10 points, the other 9 points must be satisfied before it is even appropriate to ask the subject to consent ...At 835 .*

*The Nuremberg Code is the most complete and authoritative statement of the law of informed consent to human experimentation. It is also part of international common law and may be applied, in both civil and criminal cases, by state, federal and municipal courts in the United States. However, even though the*



*courts in the United States may use the Nuremberg Code to set criminal and civil standards of conduct, none have used it in a criminal case and only a handful have even cited it in the civil context. .... Id.*

*A human subject in medical research is entitled to all material information...(Emphasis added.) Id.*

The Court of Appeals also warned that obtaining signed consents and IRB approvals will not immunize researchers from liability, especially when the subjects are children. It states:

*A researcher has a duty to inform the subject of all risks that are reasonably foreseeable...Researchers cannot ever be permitted to completely immunize themselves by reliance on consents, especially when the information furnished to the subject, or the party consenting, is incomplete in a material respect. A researcher's duty is not created by, or extinguished by, the consent of a research subject or by institutional review board approval. The duty to a vulnerable research subject is independent of consent, although the obtaining of consent is one of the duties a researcher must perform. All of this is especially so when the subjects of research are children. Such legal duties, and legal protections, might additionally be warranted because of the likely conflict of interest between the goal of the research experimenter and the health of the human subject, especially, but not exclusively, when such research is commercialized. There is always a potential substantial conflict of interest on the part of researchers as between them and the human subjects used in their research. (Emphasis supplied.) At 850.*

A commercial conflict exists for the investigators of the Children's Amalgam Study, especially those who are dentists or affiliated with dental schools or dental related organizations. While most research deals with *future* commercial applications, this study is intended to affirm a long-standing commercial enterprise: placing amalgams in millions of human beings.<sup>140</sup>

The defendants in the *Grimes* case asserted that parents have the right to consent for a child to participate in a scientific study and cited two cases in support of that proposition:

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<sup>140</sup> Those investigators who are not dentists or affiliated with the dental industry also have an economic interest in vindicating the use of amalgam. The Friends of the NIDCR, which is composed of all dental industry players (dentists, trade associations, manufacturers, dental schools and other dental related organizations), raise money to lobby Congress for ever-larger budgets for NIDCR. The Friends then lobby NIDCR for grants for favored researchers and their projects. They lobby against funding projects of researchers who have published peer-reviewed articles which link mercury amalgam to health harm. *See, for example, Andrea Rock, Mother Jones, Toxic Tipping Point, March-April 2004, pp. 73-74.*



Hart<sup>141</sup> and Strunk.<sup>142</sup> However, the court cited the cases in its opinion on behalf of the plaintiffs, stating:

*What is of primary importance to be gleaned in the Hart and Strunk cases is not that the parents or guardians consented to the medical procedures, but that they first sought permission of the courts, and received that permission, before consenting to a nontherapeutic procedure in respect to some of their minor children, but that was therapeutic to other of their children... At 855 .*

The court in *Grimes* expressed strong trepidation on guardian consents. It states:

*Courts tread cautiously when third parties are relied on to make decisions for an incapable patient. When the proposed medical course does not involve an emergency and is not for the purpose of bettering the patient's condition, or ending suffering, it may be doubtful if a surrogate decision maker--a guardian, a committee, a health-care proxy holder, a relative, or even a parent could properly give consent to permitting a ward to be used in experimental research with no prospect of direct therapeutic benefit to the patient himself. Parents may be free to become martyrs themselves. But it does not follow they are free, in identical circumstances, to make martyrs of their children before they have reached the age of full and legal discretion when they can make that choice for themselves... (Emphasis supplied.) At 855-856 .*

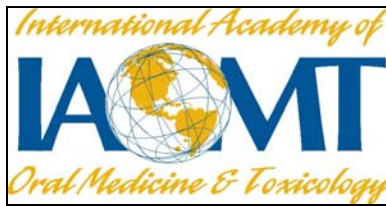
It is doubtful that any of the child-subjects were in an emergency situation with no alternative to amalgam. While dental care is generally thought of as therapeutic, such therapy has to be weighed against known harm from amalgams, which was not done here. There must also be consideration of safer, alternative treatments, which clearly do exist. And, it must be remembered that dental therapy was not the primary purpose of this study. The primary purpose was to assess the toxicity of mercury amalgam for the purpose of allowing the dental industry to continue to produce and use the cheap and easy-to-use filling material.

The similarity between the Children's Amalgam Study and the *Grimes* case is obvious: in the Children's Amalgam Study children are being used as laboratory mice to test the dose-response toxicity of a mercury – a known toxin, just as the *Grimes* child was being used to test the dose-response toxicity of lead. What distinguishes the two matters is that in *Grimes*, other children could benefit from what was learned from the lead abatement tests (though it was recognized that the primary benefit was to landlords who might be able to accomplish lead abatement more cheaply). However, in the Children's Amalgam

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<sup>141</sup> *Hart v. Brown*, 29 Conn. Supp. 368, 289 A2d 386 (1972) (court approved a parental consent for one seven-year-old twin to give a kidney to the other twin).

<sup>142</sup> *Strunk v. Strunk*, 445 SW2d 145 (Ky 1969) (court approved a parent of a mentally retarded child consenting to giving a kidney to her brother).



Study, the aim of the study is to benefit dentists who insist on using mercury amalgam as a dental filling material. There is no possibility that this study will benefit other children when continued use of mercury amalgam will assuredly contribute to their mercury body burden and all the risks associated with it.

As can be seen from this brief survey of cases arising from human experiments, liability can be assessed where consents are inadequate, where a contract exists based on the consent form, where a special relationship exists, where harm is possible or actually occurs for which no warning (or an inadequate warning) has been given, and where children and other vulnerable populations are the experiment subjects.

### **Conclusion:**

Despite the principles set out in the Nuremberg Code, federal regulations and common law, the Children's Amalgam Study has chosen subjects who may be institutionalized (Portugal), economically disadvantaged (Portugal and America) and from minority populations (Boston urban children).<sup>143</sup> Based on statements by Dr. DeRouen, it appears that the Casa Pia children have been a repeated source of study subjects because of their availability, vulnerability and lack of protectors.

White, middle-class Americans are choosing not to place mercury amalgams in their children's mouths.<sup>144</sup> It is the poor who have no choice.

The Children's Amalgam Study fails the justice principle at every level.<sup>145</sup> This study is conducted on poor, minority, handicapped and orphaned children and it belongs in the dustbin of history along with government sponsored radiation tests that began in the 1940's; WWII chemical weapons experiments involving 60,000 GI's (including 4,000 used in gas-chamber experiments that left many permanently disable – for nearly 50 years, the victims kept their secret after being told if they revealed the military experiments they would be charged with treason); the Pentagon's hallucinogen experiments (1950-1975); the Tuskegee syphilis experiments on unsuspecting black men (1932-1972); the radioactive oatmeal given to handicapped and orphaned children at

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<sup>143</sup> The presentation by Dr. Bellinger to the FDA/NIDCR scientific panel, on December 12, 2003, on mercury amalgam dental fillings, which included statistical information, stated that 37% of the child-subjects in the American portion of the study are minority children. The federal IRB regulations express special caution for use of minority research subjects. The regulations specifically provide:

*...the involvement of minorities raises concerns about the selection of subjects, the possibility of vulnerability on the part of some prospective subjects, and about consent and the relative strengths or weaknesses of vulnerable groups in the consent process. Citing 45 CFR 46.111(a)(3).*

[http://ohrp.osophs/dhhs.gov/irb\\_chapter6ii.htm](http://ohrp.osophs/dhhs.gov/irb_chapter6ii.htm)

<sup>144</sup> <http://www.health.gov/environment/amalgam2/Highlights.html> ; (Trends in use of amalgams and other restorative materials; there was a 38% reduction in amalgam between 1979-1990.)

<sup>145</sup> The Institutional Review Board Guidebook requires "justice."

[http://ohrp.osophs.dhhs.gov/irb/irb\\_introduction.htm](http://ohrp.osophs.dhhs.gov/irb/irb_introduction.htm)



Fernald School in Massachusetts (1950's); and, most infamously – the Nazi medical experiments.<sup>146</sup>

There are known safe and effective alternatives to amalgam for dental fillings. On February 6, 2004, the EPA announced that it now estimates that 630,000 children born each year – one in every eight children – are born with potentially unsafe levels of mercury in their blood.<sup>147</sup> It is immoral that the U.S. government is not engaged in minimizing mercury exposure to children from every source possible, especially the FDA and NIDCR which are especially culpable when it comes to mercury exposure from dental fillings. Every responsible organization is ascribing to the Precautionary Principle which provides that:

*When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of an activity, rather than the public, should bear the burden of proof.<sup>148</sup>*

The only reason to engage in a study to vindicate amalgam is to further the economic interests of the dental industry. Weighing dental industry economic interests, against the unnecessary addition of mercury to the body burden of powerless children is unethical, morally bankrupt and an intentional assault and battery.

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<sup>146</sup> <http://www.pcrm.org/resch/humres/humanexperiments.html> ;  
<http://www.icssc.org/Final%20presentations%20for%20CD/04%20Historical%20and%20Ethical%20Perspectives.pdf> (slide presentation on website for Data and Safety Monitoring Board on Human experiments of history).

<sup>147</sup> <http://www.ewg.org/issues/mercury/>

<sup>148</sup> <http://www.sdearthtimes.com/et0398/et0398s4.html>



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