

### Comments on “Arsenic release provided by MTA and Portland cement” by Duarte MA, et al.

*To the Editor:*

The authors presented their data from atomic absorption tests, stating that the cements released less than 0.0007 ppm of arsenic after a week of soaking in weakly acidic solution. That is, the cements released 0.7 ppb from their worst sample.

My first comment is on the atomic absorption technique for arsenic. According to the EPA method 7062 for detection of arsenic by atomic absorption using sodium borohydride reduction, the typical detection limit is 1  $\mu\text{g/L}$ , which is equal to 1 ppb. These authors are reporting amounts below the normal detection limit for the same method used by the EPA. How did they achieve such results?

Second, on page 649, the  $\text{LD}_{50}$  is listed two times for sodium arsenate as 600 mg/kg and also as 10-50 mg/kg. Which is correct? Should one of these have been sodium arsenite? Also, the authors state that they quantified trivalent arsenic, but was any pentavalent arsenic (arsenate) neglected in their analysis? Or did their analysis technique convert all pentavalent to trivalent arsenic? This should have been clarified for the reader.

Third, the authors did not report the total arsenic content of the cement they tested. In a report from the Forschungszentrum Karlsruhe GmbH, the average arsenic content of 417 Portland cements was 6.8 ppm. Another study cited in this report found an average of 33 ppm of arsenic.

Fourth, the authors did not validate their choice of a solution with a pH equal to 5, nor did they mention any of the dental standards that have solubility requirements to measure As. For instance, ISO 9917, entitled *Dental Water-based Cements*, has a requirement for lead and arsenic that is appropriate for the Portland cement and ProRoot MTA materials. In ISO 9917, the leachable lead and arsenic must be less than 100 ppm and 2 ppm, respectively. The leaching method is to use hardened, but crushed, cement in a 20% HCl solution for 16 hours. Such a solution has a pH less than 1, considerably more acidic than the authors used. Thirty-six mole percent hydrochloric acid is specified for solubility testing for arsenic in ADA 30 for zinc oxide-eugenol cement. The weakly acidic solution used by the authors did not equal the acidity of vinegar (pH of about 3). Four percent acetic acid, similar to vinegar, is the

standard used in testing the solubility of dental porcelain (ISO 9693), not cements.

Fifth, Portland cement for construction is made with waste materials. The potential for toxic metals is indicated in a sample materials safety data sheet (MSDS) for Portland cement from the Lehigh Portland Cement Company, which states that the cement “may contain trace amounts of heavy metals.” Price competition forces cement manufacturers to use the most inexpensive raw materials, including waste inorganic materials and secondary fuels such as waste oil or used tires. The raw materials and the fuels contribute heavy metals, including arsenic, lead, chromium, cadmium, and molybdenum, which become incorporated into Portland cement. The reader is referred to a report on heavy metals in cement and concrete: <http://bibliothek.fzk.de/zb/abstracts/6923.htm>. From the use of waste materials, cement-manufacturing facilities have ended up as EPA superfund clean-up sites after manufacturing ceased. An example is the Lone Star Industries site near Salt Lake City.

Portland cement is a term applied to a class of materials covering a range of compositions (containing primarily silica, alumina, and calcia). In Germany, 27 classes of Portland cement are recognized. The Portland cements vary in their properties at different compositions, as do the proportions of the phases present. If one purchases generic Portland cement, a particular composition is not guaranteed. Nor is there a guarantee about the cement’s expansion or contraction, fineness, setting time, or strength. How does a clinician know if the Portland cement from the building supply store has sufficient radiopacity, or if the particles are fine enough for handling and packing into millimeters of space? Cement used for construction does not depend on filling millimeters of space.

Last, ProRoot MTA material is, like most medical device materials, a purer grade of material than is used in industrial applications. Special medical grades of polymers and resins are used in dental restoratives and cements. The same holds true for the components of ProRoot MTA material. The composition and properties are controlled in the manufacture of ProRoot MTA root-repair material. ProRoot MTA material is specially manufactured for DENTSPLY under controlled, clean, and segregated conditions to ensure freedom from contamination (private communication with V. Gaines, DENTSPLY Tulsa Dental, January 2003).

Before a clinician uses a Portland cement as a permanent bone and dentin-contacting material that is not manufactured by a medical device manufacturer, they should consider the professional risk to use such a material. For instance, ISO 10993-1 and ISO 7405 are

documents that guide medical device manufacturers to the appropriate tests when developing a product. In ISO 7405, *Dentistry- Preclinical Evaluation of Biocompatibility of Medical Devices Used in Dentistry- Test Methods for Dental Materials*, the ProRoot MTA repair material would be classified as a permanent-contact implant device. In this category, the biocompatibility tests that are needed include cytotoxicity, genotoxicity, sensitization, implantation effects, and endodontic usage tests. ProRoot MTA has been tested for its biocompatibility using these recognized tests and for its clinical performance in humans. Does a clinician want to neglect the importance of biocompatibility testing by using something from the hardware store that has not been tested for its biocompatibility?

Clinicians know that ethical behavior is about “doing no harm” and helping patients heal; it’s not just about saving money on supplies as suggested by Saidon et al.<sup>1</sup> Using a product from a registered dental manufacturer is consistent with a dentist’s code of ethics. To suggest otherwise undermines national and international laws governing medical device manufacture, control, and quality that help us treat and protect patients.

In the United States, medical devices, including ProRoot MTA material, are manufactured under the scrutiny of engineers and scientists in facilities that are licensed and registered with the FDA and conform to FDA good manufacturing practices. The FDA requires a disclosure from manufacturers assuring the safety and efficacy testing of devices, according to appropriate ADA and ISO standards, prior to selling the medical device. A 510(k) application was submitted for ProRoot MTA material, and clearance to market the product was granted by the FDA based on testing to recognized standards. The Federal Code of Regulations also requires that manufacturers have a quality system and a vigilance system for development of a product, and surveillance of its safety and effectiveness after release to the marketplace. If inspected by the FDA, manufacturers can suffer civil and criminal penalties if their products have been adulterated. In other words, the product must be manufactured to the quality standards established under the Food, Drug and Cosmetic Act and recognized as necessary for the development of a safe and effective product. This federal system of disclosure and monitoring of manufacturing processes leads to protection of the patient and high-quality standards for products.

If a device is sold in Europe, the manufacturer’s facilities are also certified by notified bodies such as BSI or SGS to conform to the ISO 13485 specification for medical devices, and to the European Medical Device Regulation. The product design history and documentation are reviewed by the notified body, and must be approved for application of the CE mark on its packaging.

In light of the above, I am startled that the authors conclude that Portland cements are safe for use in clinical

practice in terms of the presence of arsenic. Why did they not consider other toxic metals that may have been present in their sample? Why did the authors not use a stronger acid, something generally recognized in ISO standards for testing solubility, before making such a conclusion?

This is the second article I’ve read in the OOOOE journal about ProRoot MTA material compared to Portland cement, suggesting Portland cement is safe for use instead of ProRoot MTA root canal repair material. The other article, by Saidon et al. 2003,<sup>1</sup> looked at tissue reactions but ignored other factors associated with the successful use of a root-end filling, pulp-capping, perforation, and root resorption repair material. It perplexes me that a peer-reviewed journal would accept such articles, because the authors have neglected the complexities of making and testing safe medical devices.

With these comments in mind, I suggest this journal think carefully about publishing articles that propose the use of materials that are manufactured outside of the dental industry for use in clinical practice. Clinicians should do the same before using such materials.

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#### REFERENCE

1. Saidon J, He J, Zhu Q, Safavi K, Spångberg LS. Cell and tissue reactions to mineral trioxide aggregate and Portland cement. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003;95:483-9.

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## Response to Letter to the Editor by Carolyn M. Primus, PhD

### To the Editor:

I understand there may be concerns related to the methodologies, results, and conclusions expressed in our paper. However, we believe that the basic conclusions are still correct and I would like to take this opportunity to answer the specific questions asked.

In regards to the first question, we were able to make these measurements by first adding known amounts (0.1, 0.2, and 0.3 ppb) of arsenic to the test samples in order to measure amounts that would, without these additions, normally be below detection level. The mean, the standard deviation, and the variance of the differences were calculated. The results of this evaluation allowed us to infer that this method is suitable to quantify the presence of arsenic less than the detection limit of the method.

The second question is a valid concern, as there was an oversight in correcting a typing mistake. The sodium arsenate is 600 mg/kg, and lead arsenate at 10-50 mg/kg. We quantified the trivalent arsenic because it is more toxic.

In a study by Mollah et al.,<sup>1</sup> it was demonstrated, using X-ray diffraction, that Portland cements can be considered