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The articles that follow are the latest in *Environment* Magazine's series looking back at seminal articles in the magazine's history that helped define a field of study or offered alternative explorations of new ideas. In this installment, we focus on the latest news in the hazards of the mercury toxin, juxtaposed with *Environment*'s groundbreaking article on mercury published in 1969.

Mercury Safety Reform in the 21st Century: Advancing the New Framework for Toxic Substances Control

by Oladele A. Ogunseitan

Oladele A. Ogunseitan

Citizen engagement in mercury safety reform can be strengthened through informative labels on consumer products, including nutritional supplements, batteries, and thermometers.

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The end-goal of mercury safety reform is to make routine tests for toxic mercury in consumer products obsolete and to eliminate the need to monitor mercury pollution in environments inhabited by people.

The unique physical–chemical properties of mercury have made the metal seem indispensable for applications in human health and environmental resources since antiquity. Consistent with the responsibilities of the Greek deity Hermes that bears its Roman name, mercury pollution travels transnationally, crossing environmental boundaries of water, soil, and air. Mercury is a tricky transition metal used as either poison or medicine, depending on its form. In their pursuit of fortune, artisanal miners aiming to tease gold from the earth or from electronic waste discount the well-known risks of mercury poisoning. The dangers of industrial-scale use of mercury have long been recognized, despite the wildly diverse symptoms associated with mercury poisoning, which range from physical defects to physiological malfunctions, mental health impairment, paralysis, and death. Consequently, operational guidelines and personal protective equipment have been designed for the formal occupational sector, although implementation of such interventions remains elusive in low-infrastructure regions of the world. Scientific evidence linking specific burden of disease and disability to mercury through environmental pollution or medical practice remains difficult to translate into universal protective policies.

In the United States, the long history of policy initiatives to curb mercury poisoning in the general population

The Minamata Memorial at the Minamata Disease Municipal Museum in Kumamoto Prefecture, Japan, gave its name to The United Nations' Minamata Convention on Mercury.

cuts across food consumption, energy resources, lighting infrastructure, and dentistry. At the national level, mercury is the only chemical element explicitly mentioned in the 2016 reform of the U.S. Toxic Substances Control Act (the Frank R. Lautenberg Chemical Safety for the 21st Century Act). At the international level, well-subscribed multilateral agreements such as the United Nations' Minamata Convention on Mercury address the transboundary aspects of the sources, sinks, and impacts of mercury use and pollution.[1] These initiatives have been guided in large part by increased, but incomplete, scientific understanding of the environmental life cycle of mercury and its compounds. Here, I identify gaps in translating scientific evidence to protective policies at the global level. These gaps are framed by the challenges associated with designing policy interventions within the context of scientific uncertainty; by the structure of institutional contexts for translating scientific evidence into disease prevention and environmental protection; and by the different sets of criteria used for evaluating and selecting safer alternatives to mercury. The continuing use of mercury amalgam in dentistry provides an opportunity to explore these gaps in translational science and policy development in order to reveal opportunities for advancing the goal of universal mercury safety reform.

Designing Preventive Policy Interventions With Scientific Uncertainty

The nature of scientific inquiry typically involves the widely accepted process of ongoing refinements, modifications, expansions, corrections, and paradigm shifts. The reason is partly that the instruments and methods available to researchers are continuously evolving, which means that as long as a topic remains interesting and relevant to society, the formulation of scientific questions will change to engage innovative approaches and techniques. The investigative outcome of such reframed questions may narrow margins of error, reduce uncertainty, or strengthen evidence for action in one direction or another to accomplish societal goals and aspirations. Ideally, science-based policies should also accommodate constant updates of scientific discovery, although there is inevitably a lag phase in the translational framework to settle potential disagreements in the interpretation of data, and to consider implications of

the new results for related sectors of society that may be impacted by changes in policy. Mercury biogeochemists acknowledge specific uncertainties in the scientific models of mercury cycling in the environment, particularly regarding the element's sources, reactions, receptors, and sinks in the atmosphere.[2] These gaps in scientific understanding should be transparent in negotiations to formulate domestic policies that are particularly relevant to international agreements and action plans.[3]

Dental-filling amalgam, one of the most controversial uses of mercury, is an informative example of the influence of scientific uncertainty on policy decisions. Dental amalgams consisting of approximately 40% to 50% elemental mercury mixed with powdered alloy composed of copper, silver, and tin have been used for more than a century. Numerous studies have been published about both safety and dangers of mercury amalgams used in dentistry. Claiming a thorough review of scientific evidence, the U.S. Food and Drug Administration (FDA) continues to support the use of mercury amalgam in dentistry, except for children under the age of 6 years.[4] The American Dental Association estimates that mercuric dental fillings have been used successfully in more than 100 million Americans, and considers the material to be safe, durable, and affordable.[5] The World Dental Association (FDI) also insists that exposure to mercury in various oxidation states from amalgam fillings is extremely low, and well below the limits set by the World Health Organization.[6]

Public and private agencies' narrative that mercury amalgam in dental fillings poses negligible risks to human health is challenged by individual researchers and nongovernmental advocates for public health. Those who reject the claim that dental amalgam is safe for use in humans frequently cite animal studies showing the constant leakage of mercury from dental fillings, and the use of whole-body imaging showing that the released mercury becomes localized in sensitive organs such as liver and kidney. Clinical case studies and epidemiological studies have also implicated mercury in neurological diseases such as multiple sclerosis.[7] Other investigators cite direct and indirect environmental and human health impacts of dental mercury amalgam as reasons to ban its use, including releases during cremation,[8] and the increased risk of multiple antibiotic resistance in the pathogens that infect humans because bacterial resistance to mercury is frequently transmitted through mobile genetic elements (plasmids) that also host antibiotic-resistance genes.[9] Several European countries, citing the precautionary principle, have severely restricted or banned the use of mercuric amalgams in dentistry. Still, the European Union is the world's largest user of dental mercury, consuming approximately 90 t annually.[10] In December 2016, the European Parliament, the European Commission, and the Council of the European Union agreed to ban dental mercury amalgam fillings for children younger than 15 years and for pregnant and breastfeeding women, effective July 2018. By June 30, 2020, the European Commission will

The use of mercury amalgam in dentistry is controversial because of concerns for human safety and toxic environmental pollution by wastewater from dental clinics.

report on the feasibility of a complete phase-out of mercury in dental amalgam for a later date, preferably by 2030.[11]

The scientific debate on the relative safety and dangers of dental mercury amalgam was prominent in the negotiation of the first major international policy designed to curb mercury pollution. The United Nations' Minamata Convention of 2013, the landmark international agreement to "protect the human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds," is the first international treaty to specifically include dentistry.[12] In 2005, the United States was counted among the founding partners of the United Nations Environment Programme (UNEP) Global Mercury Partnership, with aims that ultimately tracked directly to the final text of the Minamata Convention. The United States was the first country to ratify the Minamata Convention, which focused attention on mercury by building on preexisting multilateral agreements including the United Nations' Basel Convention on the Control of Transboundary Movements of Hazardous Wastes and Their Disposal, and the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. The United States has not ratified or implemented the latter two international treaties, presumably because it currently lacks the authority to implement the treaties' provisions. For this reason, the ratification of the Minamata Convention on Mercury carries particular significance for the United States' commitment to fulfill promises made under the treaty regarding both domestic agencies' responsibilities and international activities that involve trade and transportation of mercury and its products.

Although the Minamata Convention requires that member states phase out or take measures to reduce mercury used in consumer products including batteries, electrical switches, compact fluorescent lights, cosmetics, pesticides, and measuring devices, the request regarding dental amalgam is limited to creating "phase-down" initiatives designed to reduce the use of mercury. According to the U.S. Geological Survey, the leading domestic end users of mercury were the chlorine-caustic soda (chloralkali), electronics, and fluorescent-lighting industries.[13] In 2010, dental amalgam constituted the largest amount of mercury used in the United States. A study estimated that approximately 290 t of mercury in dental amalgam is contained in human mouths. An estimated 30 t of mercury amalgam was treated as waste. Although 28.5 t of mercury amalgam was released to the environment, 6 t of amalgam was recycled, and 3.5 t was treated and stored in landfills in 2009. Under the Minamata Convention, governments are required to adopt at least two of nine articulated provisions to meet the phase-down commitment regarding the use of mercury amalgam in dental care. The provisional options are: (i) setting objectives to prevent dental caries, thus minimizing the need for restorations with mercury amalgam or alternatives; (ii) setting objectives aiming at minimizing use of amalgam; (iii) promoting the use of alternatives for mercury amalgams; (iv) promoting research into alternative restorative materials; (v) promoting training in the use of mercury-free alternatives; (vi) discouraging insurance policies that favor the use of amalgam; (vii) encouraging insurance policies that favor the use of alternatives to amalgam; (viii) restricting the use of dental amalgam to its encapsulated form; and (ix) promoting the best environmental practices to reduce the release of mercury.

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Fluorescent lamps require mercury. Each lamp contains approximately 3 to 46 milligrams of mercury depending in part on the year of manufacture.

The ninth provision would have been relatively easy for the United States to adopt, but recent events compellingly illustrate the difficulty of translating scientific knowledge and technological capacity to preventive policy regarding mercury pollution. On December 15, 2016, Gina McCarthy, Administrator of the U.S. Environmental Protection Agency (EPA), signed the final rule entitled "Effluent Limitations Guidelines and Standards for the Dental Category" (PA 820-F-16-014) and submitted it for publication in the *Federal Register*. The final rule promulgates technology-based pretreatment standards under the Clean Water Act to reduce discharges of mercury from dental offices into municipal sewage treatment plants (publicly owned treatment works [POTWs]). Practically, the rule would have required installation of amalgam separators for capturing mercury in dental clinic

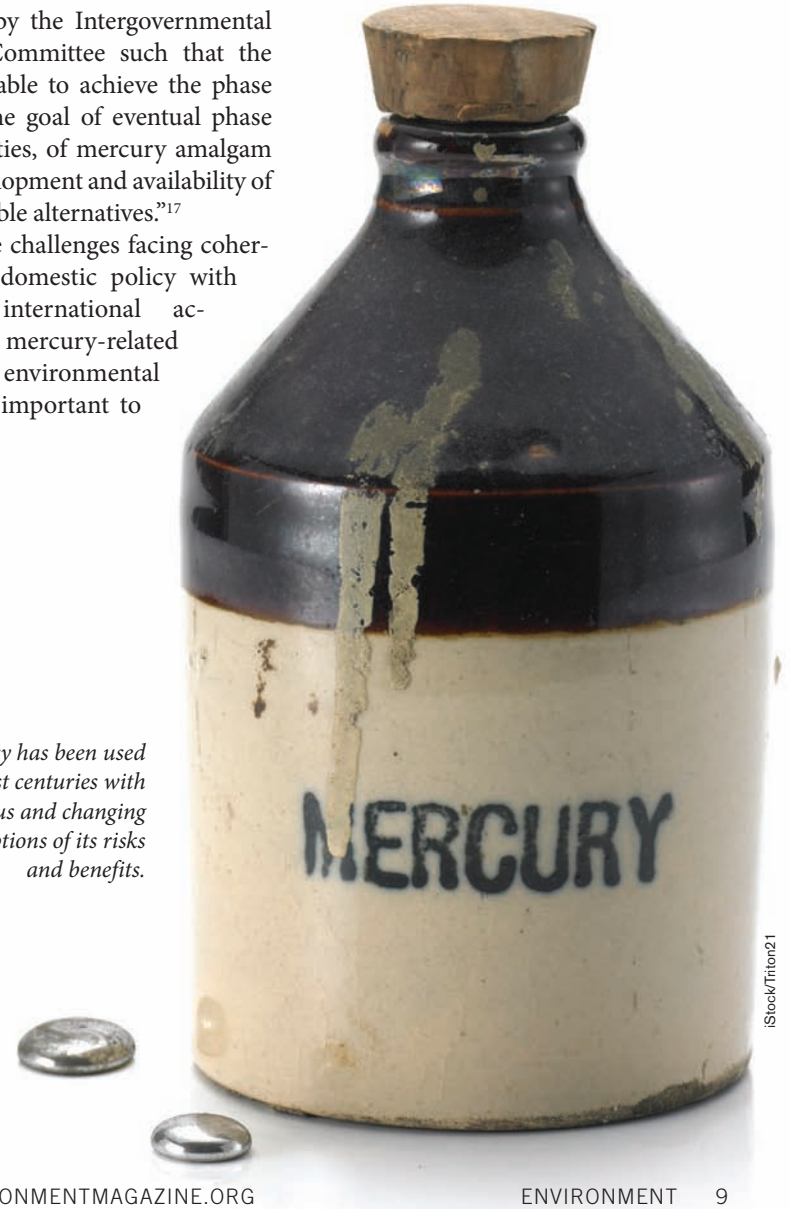
wastewater before discharge into sewers that drain to POTWs. Mercury captured by the separator is intended to be recycled. Compliance with this final rule was expected to reduce the discharge to POTWs of mercury by 5.1 tons, along with 5.3 tons of other metals found in waste dental amalgam. The EPA also estimated that the total annual cost of the final rule will be $59 to $61 million. Unfortunately, EPA withdrew the rule just before publication in the *Federal Register*, presumably because of the new federal government's declared policy to drastically reduce the number environmental regulations.[14] This unforeseen development adds a new dimension to an already incomplete understanding of the process through which scientific information and technical capacity are influenced by gaps in translational and implementation science. The institutional contexts in which scientific information is embedded can promote or retard progress, and improved analysis and understanding of such contexts are increasingly essential for domestic agencies and for multilateral international agreements.

Institutional Contexts for Translating Science to Policy

With domestic policy to reduce mercury pollution from dental mercury amalgams in jeopardy, the United States may need to pursue other provisions identified in the Minamata Convention to fulfill obligations to the international treaty. Promoting research and training on alternative "mercury-free" dental restorative materials would be relatively easy to accomplish, given the large funded research infrastructure of the United States—for example, through the National Institutes of Health's National Center for Advancing Translational Sciences. However, it is difficult to envision a vigorous research program or enthusiastic adoption of safer alternative materials without explicit support of the FDA, which has stated categorically that "any change from use of dental amalgam is likely to result in negative public health outcomes (delayed dental treatment or increased costs of treatment); while there would be a decrease in mercury exposure, there is no evidence that there would be any reduction in adverse effects associated with mercury."[15]

In a letter dated September 21, 2015, a public-interest nongovernmental organization coalition of 31 American and 29 foreign agencies called on the Secretary of the U.S. Department of State to encourage the FDA to reverse its favorable position on dental mercury amalgam, to begin supporting policies from phase-down to phase-out, and to promote the adoption of safer alternatives.[16] In representing the U.S. position during the multilateral negotiations culminating in the Minamata Convention on Mercury, the Department of State expressed support for "further consideration of dental amalgam by the Intergovernmental Negotiating Committee such that the agreement is able to achieve the phase down, with the goal of eventual phase out by all Parties, of mercury amalgam upon the development and availability of affordable, viable alternatives."[17]

Despite the challenges facing coherence of U.S. domestic policy with multilateral international actions to curb mercury-related health and environmental impacts, it is important to recognize interagency collaboration to reduce mercury impacts. However, clear gaps remain in bridging domestic policy differences and in aligning the resolution of these differences with the intent of international treaties such as the Minamata Convention. For example, mercury is singled out as the only chemical to which an entire section is dedicated in the 2016 "Frank R. Lautenberg Chemical Safety for the 21st Century Act"—the long-awaited revision of the 1975 "Toxic Substances Control Act." The Lautenberg Act calls upon the Administrator of the U.S. EPA to conduct and publish an inventory of mercury supply, use, and trade in the United States, beginning on April 1, 2017, and



Mercury has been used over past centuries with various and changing perceptions of its risks and benefits.

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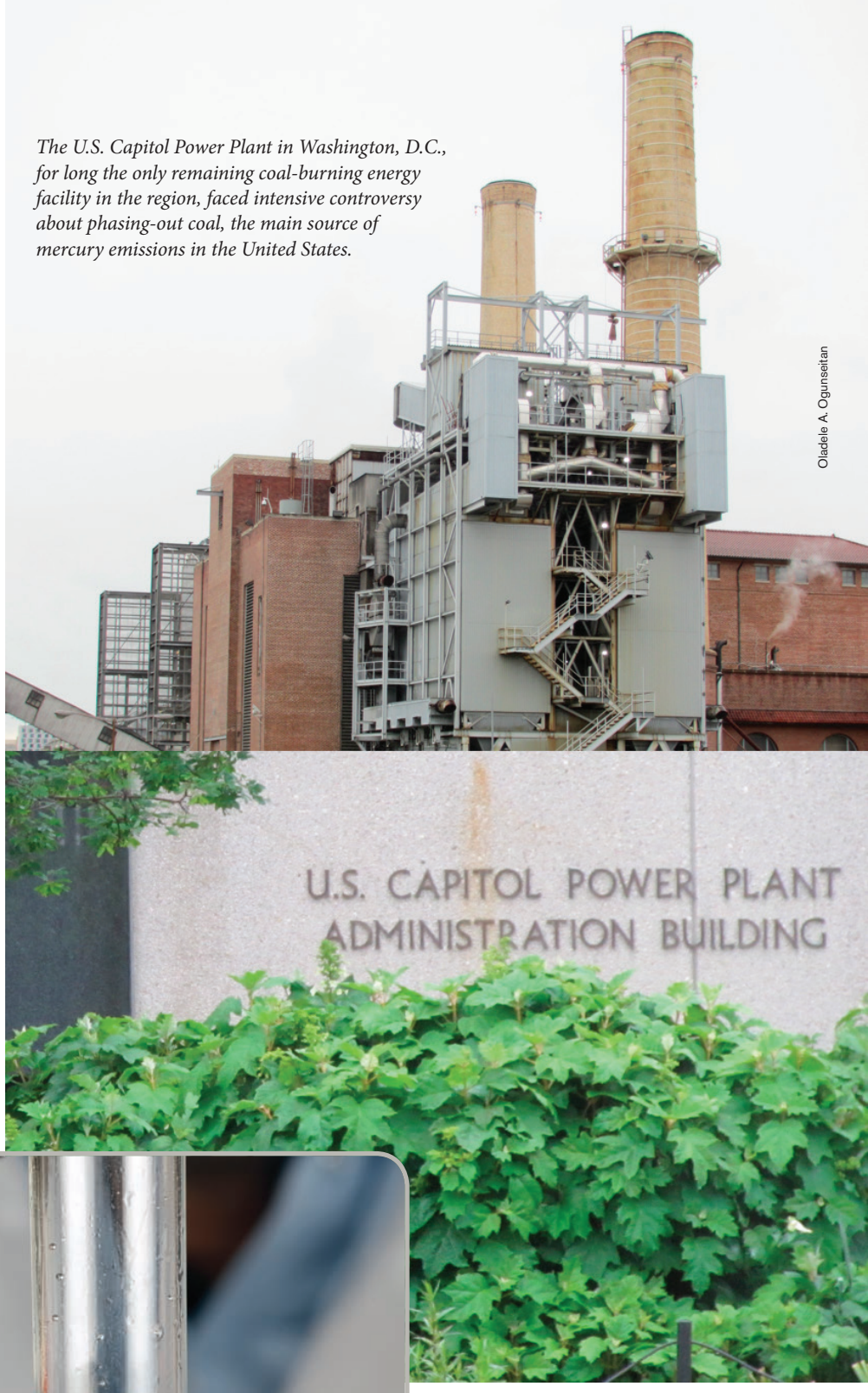
every 3 years thereafter. The required inventory specifies identification of manufacturing processes or products that intentionally add mercury, and recommendation of actions, including proposed revisions of federal law or regulations, to achieve further reductions in mercury use. However, for more than two decades, the U.S. Geological Survey has compiled and published data on mercury inventories, including production, usage, and recycling. For about the same period, the U.S. EPA has also published data on mercury emissions. It is important to explore and clarify the intent of the Lautenberg Act in the context of these historical and diversified data collection on mercury and the roles of concerned federal agencies in the process. Implementing new restrictions on mercury export will likely require collaboration of federal and state agencies, in addition to the participation of international monitoring programs. For example, section 10 under Title 1 of the Lautenberg Act expands the prohibition of mercury exportation beyond elemental mercury to include, as of January 1, 2020, mercury(I) chloride (calomel), mercury oxide, mercury sulfate, mercury nitrate, and mercury sulfide (cinnabar). These mercury compounds are mostly associated with mining and industrial activities spread across various states.



The U.S. Capitol Power Plant in Washington, D.C., for long the only remaining coal-burning energy facility in the region, faced intensive controversy about phasing-out coal, the main source of mercury emissions in the United States.

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Mercury is the only metal that exists as a liquid under room temperature and pressure. The unique feature makes mercury attractive for manufacturing, despite its toxicity.

Most of the estimated mercury consumed annually in the United States is associated with the chloralkali industries—for producing chlorine used in disinfectants—and with the electronics and electrical instruments and fluorescent-lighting manufacturing industries.[18] Regulatory policies to prevent toxic exposures and environmental contamination by mercury have also been controversial because of their linkage to energy resources, particularly coal burning, the largest source of direct mercury releases in the environment within the United States. The new federal government's inclination to increase coal mining and utilization goes against incentives to promote cleaner mercury-free energy resources. Mercury is also used to manufacture fluorescent lamps, which came into favor because of another policy action to restrict the use of high-wattage incandescent lamps for the benefit of reducing energy consumption and greenhouse gas emissions to mitigate climate change. For example, mercury was deliberately exempt from the landmark California Green Chemistry Initiative, which became the 2013 Safer Consumer Product Law.[19] In addition to the featured case of dental mercury amalgam, these other examples strengthen the argument that the convergence of U.S. domestic policies and interagency collaboration to meet commitments to the international treaty remains challenging. Different agencies seem to apply different approaches to the interpretation of scientific evidence, and to how such evidence may be translated into policies that protect populations across all states within a country, and ultimately play transformative roles in the negotiations, outcomes, and implementation of international agreements.

Bridging the Gaps by Harmonizing Criteria for Alternatives Analysis

As the only metal known to exist in liquid form under room temperature and pressure, mercury has played unique practical roles in all societies. Different constituencies clinging to the benefits of continual use of mercury, for example, in dentistry or in artisanal gold mining, claim that safer alternatives are not available, but certainly economic considerations play important roles in securing this skewed perception of benefits and risks. Mercury's persistence is remarkable despite nearly two millennia of continuous use in commerce and suspicion of its dangers. There is ample evidence of mercury's toxicity to people, wildlife, and ecosystem functions; however, the world still consumes mercury in large quantities for mining, lighting, production of chlorine disinfectant, dentistry, and manufacturing of sundry consumer products including paint (vermilion) and, to a diminishing extent, energy storage batteries. Mercury exposure is linked to various forms of disease and disability, including mental illness (mad hatter's disease) and fetal defects (Minamata disease). These health impacts have prompted numerous actions at the national and international levels to curb mercury use in commercial products and processes, despite resistance by manufacturers and some end users.

Particular scrutiny is warranted for the case regarding the international acceptance of the phase-down strategy, and the delay in phasing out dental mercury amalgam, which is attributed to the claim that alternatives are not yet available or affordable. The U.S. FDA describes two types of alternatives to dental mercury amalgams, namely, composite resin (CR) and glass ionomer cement (GIC) fillings. CR fillings are the most common alternative to mercury amalgam, and the only disadvantages indicated are that they are more difficult to place, less durable, and more expensive than mercury amalgam. The only indicated disadvantage of GIC is that they are limited to use in small dental restorations.[20] These disadvantages may seem small compared to the toxicity risks of mercury to the individual carrying dental amalgam and the environmental risks associated with the life cycle of mercury in the produc-

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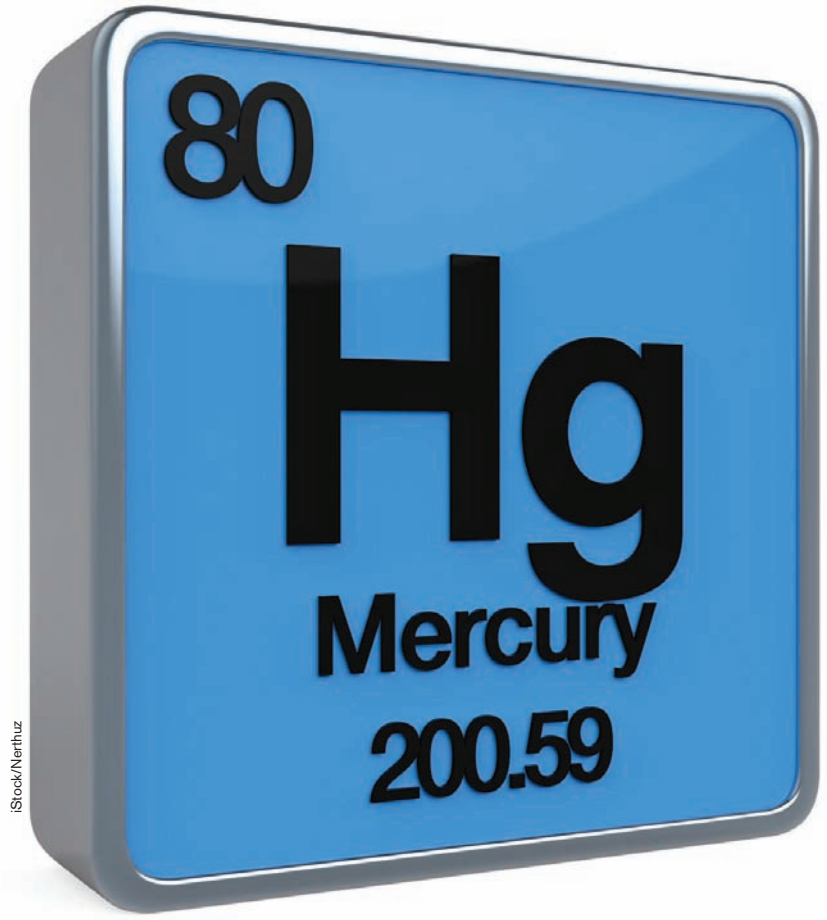
The use of mercury in artisanal gold mining is one of the largest sources of environmental pollution by mercury globally. The practice also imperils workers' health, despite the availability of alternative procedures.



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tion, installation, and disposal of amalgam. However, there are widely varied factors that weigh into the decision to adopt safer alternative materials, particularly factors of economic costs and consumer preferences based on esthetics or reputation. It is often difficult to assign uniform weights to these factors such that trade-offs are transparently acknowledged by decision makers. It is possible that regulatory top-down, command-and-control approaches can drive the innovation and the adoption of safer alternatives, but consumer preferences and willingness to pay for greener products or processes may even be more compelling. For this to happen, consumer education on the risks and benefits is crucial, and the consumers must trust the agencies promoting particular options. In this regard, it is interesting to note the difference in approach that the FDA uses regarding guidelines for limiting the consumption of fish because of mercury pollution, while on the other hand maintaining that dental mercury amalgam is safe. Interagency work to harmonize the criteria used for comparing mercury amalgam and nontoxic alternatives will contribute important information needed to educate consumers and health care professionals, and to bridge the gap between scientific evidence and policy to phase out mercury use in controversial products during the 21st century.

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NOTES

1. The United Nations' Minamata Convention is named for the first major internationally known case of mass population poisoning by mercury that occurred in Minamata city, Kumamoto prefecture, in Japan in the 1950s. Minamata disease is characterized by severe neurological damage resulting in debilitating symptoms including ataxia, loss of vision, hearing, and speech, insanity, paralysis, congenital deformity, and death within a few weeks in severe cases. The Governing Council of the United Nations Environment Programme initiated deliberations in 2009 to develop a multilateral treaty on mercury. The resulting Minamata Convention aims to protect human health and the environment from anthropogenic emissions and releases of mercury and mercury compounds, and to control mercury usage in a variety of products and processes. The convention opened for the signature of member states on 10 October 2013. The United States was the first country to ratify the Minamata Convention, on 6 November 2013. As of May 2017, there are 128 Member State signatures and 53 ratifications of the Convention, thereby satisfying the requirement for entry into force which will occur on the 90th day after the date of deposit of the 50th instrument of ratification, acceptance, approval, or accession. For additional information on the Minamata Convention, see http://www.mercuryconvention.org/Home/tabid/3360/language/en-US/Default.aspx and http://www.mercuryconvention.org/Portals/11/documents/Booklets/Minamata%20Convention%20on%20Mercury_booklet_English.pdf.

2. Examples of animal models of the adverse impacts of mercuric dental amalgams include those conducted on sheep and monkeys. See L. J. Hanh, R. Kloiber, M. J. Vimy, and F. L. Lorscheider, "Whole-Body Imaging of the Distribution of Mercury Released From Dental Fillings Into Monkey Tissues," *FASEB Journal* 4 (1991): 3256–60; M. J. Vimy, Y. Takahashi, and F. L. Lorschider, "Maternal–Fetal Distribution of 203-Hg Released From Dental Amalgam Fillings," *American Journal of Physiology—Regulatory, Integrative, and Comparative Physiology* 258 (1990): 939–45.

3. For a review of the relationships between scientific uncertainties in the atmospheric models of mercury and strategies to evaluate the potential value and real impacts of the United Nation's Minamata Convention example, see S. Y. Kwon and N. E. Selin, "Uncertainties in Atmospheric Mercury Modeling for Policy Evaluation," *Current Pollution Reports* 2, no. 2 (2016): 103–14. Although the text of the Minamata convention includes two references to "science-based," one regarding guidelines for health and the other for education, it does not include the word "uncertainty." However, as expected for well-crafted policy instruments, section 19 of the Minamata Convention articulates the need for research, development, and monitoring, aimed to improve inventories, modeling, assessments, methodologies, and information. The convention provides flexibility for member states to update their implementation plans, and there are provisions for future addition of annexes and amendments to the convention, although from the text the process is unclear through which the outcomes of scientific research will be used to update the convention's collective policy guidelines on current levels of acceptable risks that continued use of mercury, for example, at *de minimis* levels, poses to human health and environmental quality.

4. The U.S. Food and Drug Administration (FDA) guidelines for dental amalgams tout its benefits as strong and long-lasting, making dental amalgams less likely to break than some other types of fillings. In addition, dental amalgam is currently the least expensive type of filling material. The guidelines also provide information on the risks due to the release of small amounts of mercury vapor that can be inhaled and absorbed by the lungs. FDA further notes that high levels of mercury vapor exposure are associated with brain and kidney diseases. Nevertheless, FDA considers dental mercury amalgam safe, stating: "FDA has reviewed the best available scientific evidence to determine whether the low levels of mercury vapor associated with dental amalgam fillings are a

cause for concern. Based on this evidence, FDA considers dental amalgam fillings safe for adults and children ages 6 and above. The weight of credible scientific evidence reviewed by FDA does not establish an association between dental amalgam use and adverse health effects in the general population. Clinical studies in adults and children ages 6 and above have found no link between dental amalgam fillings and health problems." On 28 July 2009, FDA issued a final rule on encapsulated dental amalgam, classifying amalgam and its component parts, elemental mercury and powder alloy, as a class II medical device, which places encapsulated amalgam in the same class of devices as other less controversial dental filling materials such as composite and gold. For additional information, see https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DentalProducts/DentalAmalgam/ucm171094.htm. Given this conclusion, a question arises about the position taken by the United States in ratifying the Minamata Convention and the inherent guideline to phase down mercury-containing dental amalgam.

5. The American Dental Association (ADA) cites the 1997 consensus statement issued by the World Health Organization and the Word Federation of Dentists that "No controlled studies have been published demonstrating systemic adverse effects from amalgam restorations." Note that the absence of controlled studies is not the same as evidence for safety. ADA further states that the association has conducted a major review of the scientific literature on dental amalgam that concluded that "based on available scientific information, amalgam continues to be a safe and effective restorative material." The council's report also stated, "There currently appears to be no justification for discontinuing the use of dental amalgam." However, ADA's Council on Scientific Affairs left room for ongoing research on the safety of existing dental materials and in the development of new materials. For further information on ADA's position on dental amalgam, see http://www.ada.org/en/about-the-ada/ada-positions-policies-and-statements/statement-on-dental-amalgam. The results of a recent survey of approximately 3,000 general and pediatric dentists showed that 62% and 56%, respectively favor continued use of dental mercury amalgams. Most of the dentists surveyed agreed with installing amalgam separators to prevent environmental pollution. For details on the study, see E. Bakhurji, T. Scott, T. Mangione, and W. Sohn, "Dentists' Perspective About Dental Amalgam: Current Use and Future Direction," *Journal of Public Health Dentistry* (2017), doi:10.1111/jphd.12198.

6. The World Dental Federation (Fédération Dentaire Internationale; FDI) was founded in 1900 to advance the practice of dentistry and to discuss transnational issues, including dental education, oral hygiene, and public dental health. The federation provides position papers, best management practices, and policy guidelines to approximately 130 national associations dedicated to dentistry, such as the American Dental Association. For example, see "Understanding the Minamata Convention and Its Effect Upon Oral Health Care: Practical Advice for Dentists," http://www.fdiworldental.org/media/54670/minamata-convention_fdi-guidelines-for-successful-implementation.pdf.

7. Epidemiological studies linking dental mercury amalgam to human health effects have yielded mixed results, in part because of the sensitivity of such studies to sample size and because the general population is exposed to other sources of mercury in diet and the environment, and these are difficult to control to the level of assigning causality to dental amalgams. Also, new evidence suggests that individuals vary in their genetic susceptibility to health impacts of mercury, and until recently, the distribution of such genetic polymorphisms in the population was unknown. Nevertheless, studies questioning the conclusion that mercury amalgam is safe for everyone are abundant in the literature. Examples of notable empirical studies, reviews, and informed opinions include H. L. Needleman "Mercury in Dental Amalgam—A Neurotoxic Risk?," *Journal of the American Medical Association* 295 (2006): 1835–36; M. N. Bates, "Mercury Amalgam Dental Fillings: An Epidemiologic Assessment," *International Journal of Hygiene and Environmental Health* 209 (2006): 309–16; I. Sterzl, J. Prochazkova, P. Hrda, P. Matucha, J. Bartova, and V. Stejskal, "Removal of Dental Amalgam Decreases Anti-TPO and Anti-Tg Autoantibodies in Patients With Autoimmune Thyroiditis," *Neuroendocrinology Letters* 27 (2006): 25–30; L. T. Bello et al., "Mercury Amalgam Diffusion in Human Teeth Probed Using Femtosecond LIBS," *Applied Spectroscopy* (2017), doi:https://doi.org/10.1177/0003702816687572; U. G. Bengtsson and L. D. Hylander, "Increased Mercury Emissions From Modern Dental Amalgams," *BioMetals* (2017): 1–7, doi:10.1007/s10534-017-0004-3; F. L. Lorschieder, M. J. Vimy, and A. O. Summers, "Mercury Exposure From 'Silver' Tooth Fillings: Emerging Evidence Questions a Traditional Dental Paradigm," *FASEB Journal* 9 (1995): 504–8; M. J. Vimy, D. E. Hopper, W. W. King, and F. L. Lorscheider, "Mercury From Maternal 'Silver' Tooth Fillings in Sheep and Human Breast Milk," *Biological Trace Element Research* 56 (1997): 143–52; K. Sundseth, J. M. Pacyna, E. G. Pacyna, N. Pirrone, and R. J. Thorne, "Global Sources and Pathways of Mercury in the Context of Human Health," *International Journal of Environmental Research and Public Health* 14 (2017): 105.

8. A recent study of the relationship between bacterial resistance to mercury and antibiotics showed that bacterial resistance to multiple (three or more) antibiotics was significantly more common in mercury-resistant as compared to mercury-sensitive bacterial colonies, demonstrating co-selection of mercury and antibiotic resistances. See N.A. Lloyd, S. E. Janssen, J. R. Reinfelder, and T. Barkay, "Co-Selection of Mercury and Multiple Antibiotic Resistances in Bacteria Exposed to Mercury in the *Fundulus heteroclitus* Gut Microbiome," *Current Microbiology* 73 (2016): 834–42.

9. The Cremation Association of North America estimates that in the United States, the 2014 national rate of cremation is 46.8% with a projected increase to 52.9% by 2019. A recent study of 1,000 subjects estimates that each cremation releases approximately 2 g of mercury into the environment. See S. Myers, "Quantifying Mercury Emissions Resulting from the Cremation of Dental Amalgam in Minnesota," 2015, https://www.pca.state.mn.us/sites/default/files/aq-ei2-07a.pdf. Also see D. M. Meyer, L. M. Kaste, K. M. Lituri, S. Tomar, C. H. Fox, and P. E. Petersen, "Policy Development Fosters Collaborative Practice: The Example of the Minamata Convention on Mercury," *Dental Clinics of North America* 60, no. 4 (2016): 921–42.

10. In 2015, the European Commission's Scientific Committee on Emerging and Newly Identified Health Risks issued a final opinion on the safety of dental amalgam and alternative dental restoration materials for patients and users. The opinion focused on the scientific evidence on the potential association between amalgam and possible alternatives and adverse health effects, such as allergies and neurological disorders. The opinion cited recent in vitro evidence about the effects of mercury on developing neural brain cells and the effects of genetic polymorphism, which may enhance toxicity. Such effects have not been documented, but evidence support alteration of mercury kinetics. See https://ec.europa.eu/health/sites/health/files/scientific_committees/emerging/docs/scenihr_o_046.pdf

11. In addition to the phase-down of mercury amalgam in dentistry, the European Commission also endorsed the imposition of devices to avoid mercury from dental clinics polluting the environment. See http://www.consilium.europa.eu/en/press/press-releases/2016/12/16-mercury-pollution

12. Annex A, Part II of the Minamata Convention identifies dental amalgam as the singular mercury-added product subject to Article 4, paragraph 3 of the convention, which reads: "Each Party shall take measures for the mercury-added products listed in Part II of Annex A in accordance with the provisions set out there in." The first paragraph of Article 4 specifies that "Each Party shall not allow, by taking appropriate measures, the manufacture, import or export of mercury-added products listed in Part I of Annex A after the phase-out date specified for those products, except where an exclusion is specified in Annex A or the Party has a registered exemption pursuant to Article 6."

13. For nearly two decades, the U.S. Geological Survey has published annual reports on estimates covering mercury industry data. The information includes domestic industry structure, government initiatives and programs, tariffs, and salient statistics. See "Mercury Statistics and Information" (prepared by Micheal George), https://minerals.usgs.gov/minerals/pubs/commodity/mercury/mcs-2017-mercu.pdf

14. For a copy of the final rule on the installation of mercury separators in dental clinics, see https://www.epa.gov/sites/production/files/2016-12/documents/dental-office-category_final_prepub_12-15-2016.pdf. For notification on the withdrawal of the rule, see https://www.epa.gov/eg/dental-effluent-guidelines. The Natural Resources Defense Council (NRDC) consequently sued the EPA in a complaint filed on 1 February 2017 charging that the mercury rule could not be withdrawn just before publication in the *Federal Register* because it is not a "new" regulation; rather, it is linked to the existing Clean Water Act. See *NRDC v. EPA et al.,* at U.S. District Court, Southern District of New York, No. 17-00751; see http://www.jurist.org/paperchase/NRDC%20complaint.pdf.

15. See U.S. Department of Health and Human Services, *Federal Register*, 74 FR 38707-08, dated 4 August 2009, https://www.gpo.gov/fdsys/pkg/FR-2009-08-27/content-detail.html

16. For a copy of the nongovernmental organization letter to Secretary John Kerry see: "Mercury Policy Project: Promoting Policies to Eliminate Mercury use and Reduce Mercury Exposure," http://mercurypolicy.org/wp-content/uploads/2015/09/sec_state_kerry_ngo_letter_sept_21_2015.pdf

17. The U.S. Department of State also conveyed to the international negotiating committee that "The United States has already taken significant steps to reduce the amount of mercury generated and released into the environment, and can implement Convention obligations under existing law." If the current regulatory impasse persists, the situation with mercury amalgam may prove to be an exception to this assurance. For the full text of the U.S. government submission to the Mercury International Negotiating Committee, see http://www.unep.org/hazardoussubstances/Portals/9/Mercury/Documents/INC3/United%20States.pdf

18. The U.S. Geological Survey (USGS) is the authoritative source on the sources and sinks of mercury demand in the United States, and has compiled extensive trend data that reveal the impacts of policy on imports and exports, which ultimately influence risks to the population. For the USGS database on mercury, see "Mercury Statistics and Information (Mineral Commodity Summaries, Prepared by Micheal W. George)," https://minerals.usgs.gov/minerals/pubs/commodity/mercury/mcs-2016-mercu.pdf

19. The landmark California Safer Consumer Products Law emerged from several years of deliberation and consultation structured around the Green Chemistry Initiative. The law was eventually implemented in the term of Governor Arnold Schwarzenegger, and it is distinctive for its emphasis on the requirement for alternatives analysis. For additional information on the law, see "California Department of Toxic Substances Control—Safer Consumer Products," http://www.dtsc.ca.gov/LawsRegsPolicies/Regs/SCPA.cfm (see ftp://www.leginfo.ca.gov/pub/0910/bill/asm/ab_1051-1100/ab_1078_cfa_20090427_122151_asm_comm.html).

20. The U.S. Food and Drug Administration publicizes brief notes on alternatives to mercury amalgam, but does not use safety as a criterion for ranking the alternatives. See https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DentalProducts/DentalAmalgam/ucm171108.htm#1. The International Academy of Oral Medicine and Toxicology lists several additional alternatives with particular information on safety. These include porcelain and gold. Moreover, the academy rejects the conclusion that the "safer" alternatives are less durable than mercury amalgam. For additional information, see https://iaomt.org/for-patients/alternatives-mercury-amalgam-fillings.