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Thimerosal as discrimination: vaccine disparity in the UN Minamata Convention on mercury

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Abstract

When addressing toxins, one unmistakable parallel exists between biology and politics: developing children and developing nations are those most vulnerable to toxic exposures. This disturbing parallel is the subject of this critical review, which examines the use and distribution of the mercury (Hg)-based compound, thimerosal, in vaccines. Developed in 1927, thimerosal is 49.55% Hg by weight and breaks down in the body into ethyl-Hg chloride, ethyl-Hg hydroxide and sodium thiosalicylate. Since the early 1930s, there has been evidence indicating that thimerosal poses a hazard to the health of human beings and is ineffective as an antimicrobial agent. While children in the developed and predominantly western nations receive doses of mostly no-thimerosal and reduced-thimerosal vaccines, children in the developing nations receive many doses of several unreduced thimerosal-containing vaccines (TCVs). Thus, thimerosal has continued to be a part of the global vaccine supply and its acceptability as a component of vaccine formulations remained unchallenged until 2010, when the United Nations (UN), through the UN Environment Programme, began negotiations to write the global, legally binding Minamata Convention on Hg. During the negotiations, TCVs were dropped from the list of Hg-containing products to be regulated. Consequently, a double standard in vaccine safety, which previously existed due to ignorance and economic reasons, has now been institutionalised as global policy. Ultimately, the Minamata Convention on Hg has sanctioned the inequitable distribution of thimerosal by specifically exempting TCVs from regulation, condoning a two-tier standard of vaccine safety: a predominantly no-thimerosal and reduced-thimerosal standard for developed nations and a predominantly thimerosal-containing one for developing nations. This disparity must now be evaluated urgently as a potential form of institutionalised discrimination.

Introduction

At its 25th session on February 29, 2009, the Governing Council of the United Nations Environmental Programme (UNEP) agreed to the formulation of a global, legally binding instrument on mercury (Hg) and asked the executive director of the UNEP to form an intergovernmental negotiating committee (INC) with the mandate of preparing that instrument (1). In 2010, the INC was formed and it began negotiations that spanned five sessions. The legally binding instrument (eventually termed the Minamata Convention on Hg) was negotiated by the INC1 from June 7 to 11, 2010 in Stockholm, Sweden; the INC2 from January 24 to 28, 2011 in Chiba, Japan; the INC3 from October 31 to November 4, 2011 in Nairobi, Kenya; the INC4 from June 27 to July 2, 2012 in Punta del Este, Uruguay; and the INC5 from January 13 to 18, 2013 in Geneva, Switzerland (2). The text of the Minamata Convention on Hg was adopted, then opened for signature at a diplomatic conference in Minamata and Kumamoto, Japan from October 9 to 11, 2013 (3).

The Minamata Convention on Hg specifically recognises that Hg, in all its forms, is a substance of global concern because it can have significant negative effects on human health. It acknowledges that this is especially relevant to developing countries, where vulnerable populations, including women and children, and through them, the future generations are more likely to be harmed through exposure to Hg (3). As a result, the Minamata Convention on Hg states that its objective is to protect human health from exposure to Hg and Hg compounds. In keeping with this objective, it places extensive restrictions on the sources that supply and trade in Hg, Hg-added products, manufacturing processes in which Hg and Hg compounds are used, artisanal and small-scale gold mining, Hg emissions, and Hg wastes. Further, it mentions financial and technological resources and sets out mechanisms to avoid the use of Hg, protect vulnerable populations from Hg intoxication, facilitate the exchange of scientific information on Hg toxicity, and facilitate the education of the public and the dissemination of information to the public on Hg toxicity (3).

With respect to Hg-containing products, the INC sessions were tasked with developing a comprehensive and suitable approach to the use of Hg that included: reducing the supply of Hg and enhancing the capacity for the environmentally sound storage and use of Hg; reducing the demand for Hg in products and processes; reducing international trade in Hg; increasing the knowledge of the use of Hg through awareness-raising activities and scientific information exchanges; specifying arrangements for capability-building, including technical and financial assistance to developing countries; and addressing the issue of compliance. Despite all the aforementioned goals, in its final form, the Minamata Convention on Hg exempted thimerosal-containing vaccines (TCVs) from regulation.

During the INC sessions, there were vigorous discussions on the presence of thimerosal in the global vaccine supply and intense debates over whether it would be regulated or exempted from regulation in the diplomatic instrument. Thimerosal (a trade name for sodium ethylmercurithiosalicylate) is also known as merthiolate, thiomersal, timerosal and tiomersal. Developed in 1927, it is 49.55% Hg by weight and is rapidly broken down into ethyl-Hg chloride, ethyl-Hg hydroxide and sodium thiosalicylate in aqueous saline environments, such as those found in vaccines and the human body (4). Despite evidence dating back to the early 1930s that thimerosal is hazardous to human health and ineffective as an antimicrobial agent, it continued to be a part of the vaccine supply and its acceptability as a global component of vaccine formulations remained unchallenged until the INC negotiations (5). The controversy surrounding thimerosal and the fact that ultimately, it was specifically exempted from regulation by the Minamata Convention on Hg must now be scrutinised as the Convention has sanctioned the continuation of the disparity, with the global distribution of TCVs remaining uneven. Since there is a discernible and inverse relationship between the wealth of a nation and the Hg content of its vaccines for children, the question of whether this disparity is ethical demands an urgent answer.

A double standard in vaccine safety?

As in biology, so too in politics: just as toxic exposures affect developing children much more than mature adults, toxic exposures affect developing nations much more than developed ones. Developing nations, whose children are being exposed to Hg through the administration of vaccines at a higher rate and greater frequency than children in developed nations, risk having the intellectual potential of their next generation diminished at a point in their national development when they can least afford it. In addition, they usually lack the resources to police their borders, identify toxic products, and shift global policies that are shaped by the interests, and even the conflict of interests, of developed nations. Like children who have biologically immature detoxification systems and cannot defend themselves against the injection of thimerosal into their bodies as part of a vaccine, developing nations, with their dearth of resources, alternatives and expertise, are unable to defend themselves against toxic substances introduced through their borders due to an exemption in a diplomatic instrument. While Hg exposure is harmful in all cases, countless ethical questions arise from the fact that it is developing children in the developing nations who are disproportionately vulnerable to the potential hazards of TCVs. A notable exception is the USA where thimerosal continues to be used in inactivated influenza vaccines that may be administered to pregnant women and developing children. The reason for this, critics allege, is to justify the use of thimerosal in those developing nations where the laws and regulations are keyed to US ones. The disparity between developed and developing nations with respect to TCVs cannot be ignored in any evaluation of the historic impact, both positive and negative, of the Minamata Convention on Hg.

As the Minamata Convention on Hg was being negotiated, civil society representatives from the Coalition for Mercury-free Drugs (CoMeD), a participating non-governmental organisation (NGO) (6), argued that this disparity constitutes an obviously discriminatory double standard in vaccine safety, which some have attempted to justify (7). While proponents of thimerosal acknowledged that such a disparity does, indeed, exist between high-income countries (HICs) and low- and middle-income countries (LMICs), they offered three main arguments to defend the exemption of TCVs from regulation (8). They argued that first, the use of thimerosal as a vaccine preservative is safe, and its removal from most of the thimerosal-preserved vaccines in the HICs was merely precautionary. Their second argument was that cold-chain and storage issues make it impossible to remove thimerosal from the multi-dose vaccine formulae intended for LMICs, because there is no "viable" alternative for thimerosal as a preservative in these formulations. Third, they argued that justice lies in providing the LMICs with thimerosal-containing multi-dose vaccines rather than no vaccines at all. The validity of each of these arguments will be evaluated.

Before analysing these arguments, however, it is of critical importance to make a preliminary assessment of the ultimate "moral" conclusion predicated upon these claims [emphasis added]: "Treating individuals with equal regard, however, does not mean that *all people are treated the same in all respects* …. It is only when differences in practice are not justified by differences in the need and circumstances of the target individual or group, leading to avoidable harm, that concerns of injustice and inequality arise" (8).

The preceding quote contains the justification mentioned earlier – that differences in circumstance justify differences in treatment. This argument was used by the opponents of many historical movements for social justice in the twentieth century (9). In the case of TCVs, should the income level of a nation impact the types of vaccine formulations it receives? Does the low income level of a nation justify a much higher level of a known neurotoxin in vaccines intended for its children than the level in nations with a higher income? Are all nations and all children not equally entitled to the protection of the precautionary principle? And should the precautionary principle not apply especially to those who are developing, be they individuals or nations, given their particular vulnerability? The argument put forward in 1934 by the US President, Franklin Delano Roosevelt, that no country, however rich, can afford to waste its human resources, and the obvious corollary of this argument, that every country, regardless of how developed it is, must guard against the wasting of its intellectual resources, must now be considered.

After examining the issues of disparity, toxicity and inequity with reference to the current distribution of thimerosal, this critical review will consider whether the specific exemption of TCVs from regulation, despite the fact that in many early drafts of the treaty, they were included in a list of Hg-containing products to be regulated, constitutes a tacit endorsement of a

two-tier standard of vaccine safety based on national wealth. If this is true, then the Minamata Convention on Hg can be described as a historic instance of global discrimination against developing children in developing nations and is violating essential elements of the right to health, including "accessibility", as described by the United Nations [emphasis added]: "Health facilities, goods and services must be accessible to all, especially the most vulnerable or marginalised sections of the population, in law and in fact, *without discrimination*…" (10).

Documenting disparity in the thimerosal content of vaccines for HICs and LMICs

Among the health authorities, there seems to be no dispute that, unlike the HICs, the LMICs still receive essential early childhood vaccines in which thimerosal is used as a preservative or a production aid. While the disparity is widely recognised, a nation-by-nation listing of the nominal Hg content of all TCVs is not readily available in the public domain. A survey of the vaccines being marketed currently, however, allows us to make a useful comparison between the Hg content of thimerosal in some of the vaccines distributed in the HICs and the Hg content of similar vaccines distributed in the LMICs. This comparison is summarised in Table 1.

Opposing the regulation of TCVs by the treaty, the American Academy of Pediatrics (AAP), a professional guild organisation of American physicians, joined the World Health Organisation (WHO) in urging the UN to drop the proposed regulation because [emphasis added] "…the Thimerosal ban could keep children *in poor nations* from getting needed vaccines" (11). To justify this disparity, the AAP, in agreement with WHO, suggested that it is essential for vaccines to contain thimerosal. Furthermore, AAP suggested that the call it had made in 1999 for the removal of thimerosal from vaccines as soon as possible was a mistake. The AAP stated that on the basis of select research conducted since 1999 (12), it would now be inconceivable for it to join the United States Public Health Service in issuing such a statement (11,13). Instead, in direct opposition to its earlier position, the AAP publicly argued during the INC negotiations that thimerosal *must* remain in vaccines. Supporting the WHO recommendation to delete the proposed ban on thimerosal from the drafts of the Minamata Convention on Hg, it claimed that such a ban would do tremendous damage to current vaccine programmes that would otherwise protect all children from death and disability caused by vaccine-preventable diseases (11,13).

The NGOs, on the other hand, stressed that the removal of thimerosal from the early childhood vaccines in the USA (12), western Europe, Scandinavia and various other nations (14) had placed children in the LMICs at a disproportionately elevated risk of being harmed, should thimerosal pose a real risk of harm. US health officials had anticipated this disparity as early as 1999, when Peter Patriarca of the US Food and Drug Administration (FDA) had written to Lawrence Bachorik, predicting, "…You should also be aware that if the US (and perhaps the EU) adopts a position that the theoretical risk of ethyl mercury exposure outweigh(s) its potential benefits to the point where no vaccines used in the US or Europe will contain thimerosal (which is where things appear to be headed), this could also have a severe impact on global ('third world') vaccination programmes, particularly for hepatitis B and whole-cell DTP vaccines, which, for various reasons, will almost certainly have to have thimerosal as an ingredient for potentially many years to come. WHO has already made a plea to the American Academy of Pediatrics to 'tread lightly' and 'consider the global ramifications' of their evolving policy… I'm not sure if there will be an easy way out of the potential perception that the FDA, CDC and immunisation policy bodies may have been 'asleep at the switch' re: thimerosal until now" (15). Acknowledging on December 17, 2012 that the USA had reduced the amount of thimerosal in most of its vaccines or removed it altogether, Walt Orenstein, the former director of the US Centers for Disease Control and Prevention (CDC) National Immunization Program, admitted, "I don't see any reason that the US would add thimerosal back into childhood vaccines…" (16). Having established that there is a disparity in the global distribution of thimerosal through TCVs to HICs and LMICs, it is now imperative to examine the toxicity of thimerosal and the risk it poses to those who routinely receive TCVs in LMICs, especially developing children.

Is thimerosal safe and was its removal from vaccines for the HICs merely precautionary?

The US federal record on thimerosal

In its submission to the INC of the United Nations Environment Programme (UNEP), a US government delegation led by Dr John E Thompson, the Deputy Director of the Office of Environmental Policy for the US State Department, informed the INC delegates, "In summary, licensed vaccines containing thimerosal preservative have been determined to be safe and effective under the applicable US statutory and regulatory requirements and therefore, are approved for use in the United States" (17). This blanket statement neither acknowledged the availability of stocks of thimerosal-free and thimerosal-reduced vaccines in the HICs, nor did it acknowledge other significant and troubling federal statements that had disputed the safety of thimerosal.

In 2004, the then US Special Counsel, Scott Bloch, called for a Congressional investigation into the use of thimerosal in vaccines after receiving hundreds of complaints by citizens that their children had been harmed by TCVs (18). In contrast to the position taken by the US delegation in its submission to the UNEP, and after a thorough investigation into the matter, Bloch found that "…based on the publicly available information…, it appears there may be sufficient evidence to find a substantial likelihood of a substantial and specific danger to public health caused by the use of thimerosal/mercury in vaccines because of its inherent toxicity" (18). Bloch also characterised TCVs as [emphasis added] "a far-reaching public health issue that warrants further study and awareness,

particularly because it affects *the most vulnerable* among us" (18). When speaking of "the most vulnerable among us." he was referring to foetuses and newborn infants who, because of their rapid neurological development, immature immune, digestive and detoxification systems, and very low body weight, are the most susceptible to the harmful effects of a toxic exposure at any level.

The US delegation to the INC also failed to quote the findings of the Subcommittee on Human Rights and Wellness, of the Committee on Government Reform, United States House of Representatives, chaired by Congressman Dan Burton. In May 2003, the subcommittee had issued a Congressional report that stated: "Thimerosal used as a preservative in vaccines is likely related to the autism epidemic. This epidemic in all probability may have been prevented or curtailed had the FDA not been asleep at the switch regarding the lack of safety data regarding injected thimerosal and the sharp rise of infant exposure to this known neurotoxin" (15).

These official government statements cast a doubt on the certainty with which the US delegation to the INC claimed that thimerosal was safe. Dr Thompson acknowledged that this claim was shaped by the stance of the US FDA, the agency considered to be "expert" on the issue and the agency subordinate to the US Department of Health and Human Services, which incidentally has been the "defendant" in more than 5000 petitions alleging vaccine-induced harm before the US National Vaccine Injury Compensation Program (NVICP) (19).

The US delegation's claim regarding the safety of thimerosal is, in fact, far more extreme than even that of the manufacturers of thimerosal. For example, the material safety data sheet for thimerosal published by its manufacturer, Eli Lilly and Company (Indianapolis, IN, USA), reveals that the "effects of exposure may include numbness of extremities, fetal changes, decreased offspring survival, and lung tissue changes...*in utero and in children* may cause mild to severe mental retardation and mild to severe motor coordination impairment" (20). Thimerosal is so toxic that in the USA, its use as an ingredient in over-the-counter topical antiseptics, diaper-rash products and spermicides has been illegal since 1998 (21). Given the fact that thimerosal is too toxic to apply to the skin or use as a contraceptive, one must ask how it can be safe to inject it directly into the body and blood of a developing child or pregnant woman.

The scientific record on thimerosal

Neither the federal, nor the scientific record supports the position of the health authorities involved in the UNEP negotiations that "avoidable harm" is not associated with TCVs. When assessing the safety of thimerosal, it is important to remember that not even one modern human clinical safety trial has been undertaken to evaluate it (15). Instead, the idea that it is "safe" is based on the findings of a single crude human experiment which was carried out in 1929 and which resulted in the deaths of all 22 persons to whom thimerosal was administered (15). While most of the subjects died within a day or two of the administration of thimerosal, the doctor overseeing the study, financed by the patent-holding manufacturer of thimerosal (then called merthiolate in the USA), attributed each of these deaths to bacterial meningitis, the condition that thimerosal was being used to treat. The physician, Dr KC Smithburn, then declared that thimerosal was ineffective for the treatment of meningitis but "safe" for intravenous administration in humans, although at the concentration used, it caused tissue death when accidentally infused into a patient's muscle tissue rather than a vein. Despite Smithburn's initial claim of "safety", serious concerns were raised about the use of thimerosal in serum products as early as 1935, when the Pittman Moore company determined that it was not suitable for use as a preservative in serum administered to dogs (15).

Perhaps the most important evidence of the toxicity of thimerosal was provided by Nelson and Gottshall from the Division of Biologic Products, Bureau of Laboratories, Michigan Department of Public Health (a manufacturer of pertussis vaccines) when they assessed its safety in vaccines using the well-established mouse toxicity test in 1967 (22). They evaluated the toxicity of pertussis vaccines by injecting mice intra-abdominally with a suspension of the vaccine, diluted in physiological saline, and then observing changes in weight and mortality. In the course of preparing and testing the vaccines, the researchers observed that they were less toxic for mice when diluted in saline than in saline containing thimerosal at a final concentration of 1:10,000 (0.01%), the same nominal concentration found in most TCVs being administered to children today. Pertussis vaccines preserved with 0.01% thimerosal were more toxic for mice than were unpreserved vaccines prepared from the same parent concentrate and containing the same number of organisms. In addition, an increase in mortality was observed when thimerosal was injected separately, before or after an unpreserved saline suspension of pertussis vaccine. These results confounded the expectations of Nelson and Gottshall because, given the widespread use of thimerosal to preserve pertussis vaccine, these researchers had assumed it would be safe. Such early and substantial warnings about thimerosal seem to have been both ignored and forgotten by those who advocate the continued use of thimerosal in vaccines, claiming that there is no credible scientific evidence that its use in vaccines presents a risk to human health (8).

Such "amnesia" is also evident in the industry-sponsored studies that have been carried out in the last 70 years (5), but this phenomenon is not limited to the past. A landmark US CDC study which found evidence of the significant harm caused by TCVs went unpublicised, even though it was presented to a conference of the Epidemic Intelligence Service in 2000 (23). In this study, US CDC epidemiologists, including the lead researcher and Epidemic Intelligence Service officer, Thomas Verstraeten, and his colleagues, assessed the risk of neurological and renal impairment associated with past exposure to TCVs, using automated data from the Vaccine Safety Datalink (VSD). The data sets

reviewed consisted of information on patients "from four health maintenance organizations (HMOs) in Washington, Oregon, and California, containing immunization, medical visit, and demographic data on over 400,000 infants born between 1991 and 1997" (23). The investigators categorised the cumulative nominal exposure to Hg from TCVs after one month of life and assessed the subsequent risk of diagnosed degenerative and developmental neurological and renal disorders before the enrolled children reached six years of age. They applied proportional hazard models, adjusting for the health maintenance organisation and the enrolled children's year of birth and gender, and they excluded premature babies. The results showed that "the relative risk (RR) of developing a neurologic developmental disorder was 1.8 (95% confidence interval [CI]=1.1–2.8) when comparing the highest exposure group at 1 month of age (cumulative dose >25 µg of Hg) to the unexposed group (23). Within this highest exposure group, the authors of the study also "found an elevated risk for the following disorders: autism (RR 7.6, 95% CI=1.8–31.5), non-organic sleep disorders (RR 5.0, 95% CI=1.6–15.9), and speech disorders (RR 2.1, 95% CI=1.1–4.0)" (23). Similarly, other investigators examined a cohort of 278,624 subjects born between 1990 and 1996 within the Vaccine Safety Datalink (24). These investigators found that increasing exposure of infants to Hg from TCVs was associated with a significantly elevated risk of autism, autism spectrum disorders, learning/ developmental disorders, tics, attention deficit disorder and emotional disturbances.

That children are extremely sensitive to thimerosal has been documented since at least 1977 (25). In that year, a study was carried out in which thimerosal was added topologically to the stomach area of 13 children with infected umbilical cords, after which 10 of them died. According to the autopsy report, the deaths were due to the effects of internal organic Hg toxicity. This study is a stark illustration of the reality that infants and young children are much more susceptible to the toxic effects of thimerosal than older children and adults. Nonetheless, infants are exposed to significant levels of Hg through TCVs even today, and an estimated 50% of the Hg many infants receive comes from periodic bolus doses of thimerosal in certain vaccines (26,27). Overall, it has been estimated that some infants may by exposed to about 164 µg of dietary Hg (from breast milk) and a cumulative dose of organic Hg from TCVs exceeding 187.5 µg, all in the first six months of life (27). From the late 1980s through the early 2000s, thimerosal from vaccines contributed significantly to the exposure of some American infants to Hg levels that exceeded the safety limits set by the US Environmental Protection Agency (EPA), US FDA, US CDC and WHO (27). In clinical studies on human infants, the administration of TCVs has been observed to lead to Hg levels in the blood and hair that are in excess of the safety limits established by the EPA (28–31). In addition, animal studies which examined the administration of Thimerosal, mimicking the infant vaccine schedule of the USA in the 1990s, have also revealed that it has significant adverse neurodevelopmental consequences in rats, mice and monkeys (32–37). Therefore, the presence of thimerosal in vaccines specifically intended for young infants is both illogical and obviously dangerous.

In addition to the establishment of the fact that thimerosal is harmful for foetuses and young children, as well as animals, the process and biochemical mechanisms through which this harm is caused are now being described (26). The latest research on the subject describes how "for each child and every exposure, there is a unique set of factors, the sum of which govern whether there will be adverse effects from a toxic exposure (to thimerosal), and if so, how severe. The unique nature of individual exposure is made even more complex by subsequent exposures and the individual body's ability to excrete some of that Hg prior to the next exposure … depending on thiol content and availability. A historic and intricate understanding of a toxic exposure and its many contributing and interacting factors, which culminate in determining outcome and adverse effects, is now emerging" (26).

Emerging science from developing countries

In recent years, in addition to the aforementioned studies from developed countries, studies have been undertaken to quantify the risk of harm from the administration of TCV to children in developing countries. For example, investigators examined how exposure to Hg through TCVs administered within the first six months of life affected the neurodevelopment of Amazonian infants in one urban centre and two rural villages (38). They found that such exposure had a significant and increasingly negative impact on Gesell development scores with increasing amounts of Hg exposure from TCVs administered within the first six months of life. Other investigators examined a cohort of infants in Poland to evaluate the relationship between neonatal exposure to the administration of TCVs and child development (39). They observed that the administration of TCVs had a significant impact on psychomotor development between the 12th and 24th months of life, and that over the course of three years of follow-up, the overall deficit in psychomotor development attributable to neonatal exposure to TCVs was significantly higher in the group exposed to TCVs.

That the harm caused by thimerosal was comprehensively documented just one year before the Minamata Convention on Hg exempted TCVs from regulation globally is tragically ironic. It would seem that the assurances offered by the HICs to the LMICs regarding the safety of the use of thimerosal in vaccines were misguided at best and deceptive at worst. It is also ironic that those who led the diplomatic effort in favour of retaining thimerosal in vaccines for the LMICs are predominantly HICs (including the USA). Many of these HICs, in fact, participate in the activities of, or are allied to, the JUSSCANZ (a negotiating block, the members of which are Japan, the USA, Switzerland, Canada, Australia, Norway and New Zealand) working group of the INC, and have already reduced and/or removed thimerosal from all, or almost all, their own paediatric vaccine formulations.

Having established that the safety of thimerosal is in dispute, and that this dispute dates back to the 1930s, the argument that thimerosal was removed from vaccines marketed in the HICs merely as a precaution must be discounted. In summary, if thimerosal is most likely associated with an avoidable, serious and documented risk of harm, it is of paramount importance to find out whether an effective, safer alternative exists.

Is removing thimerosal from vaccines for LMICs impossible due to cold-chain and storage issues and the lack of any alternative to thimerosal for multi-dose vials?

Can it be that since 1929, the development of a more effective, less toxic preservative has eluded science? Moreover, if an alternative does exist, why were the deliberations of the INC, which wrote the text of the Minamata Convention on Hg, dominated by arguments claiming that there is no injustice in allowing the use of thimerosal in vaccines due to the lack of any alternative. Instead, the proponents of thimerosal argue that the real threat of injustice comes from the contemplation of removing "this currently necessary and irreplaceable compound" from the global vaccine supply (8).

Arguments that thimerosal is essential due to the limitations of cold-chain storage capability and the lack of an effective, alternative preservative are difficult to sustain when the use of the safer, much less toxic and more effective preservative, 2-phenoxyethanol (2-PE) in the HICs, is given careful consideration. This preservative is the alternative of choice for multi-dose vials in the HICs (40), notwithstanding the claim made by the US delegation to the INC that the use of 2-PE is experimental and its recommendation that thimerosal must continue to be used in the developing nations: "The FDA has not identified any preservative as effective as thimerosal preservative. Some have suggested the use of 2-phenoxyethanol as an alternative; however, this component has not been widely used as a preservative in US-licensed vaccines and, for some vaccines, it was shown not to be effective when used alone as a preservative" (17).

While many have claimed that the effectiveness of thimerosal is singular and that this justifies its continued use and exemption from regulation by the Minamata Convention on Hg, one definitive scientific study, sponsored by the drug manufacturer, Pfizer, when developing a multi-dose Prevnar/ Prevenar™ vaccine formulation, clearly contradicts these claims. The investigators described the development of a Prev(e)nar 13™ multi-dose vaccine formulation intended to vaccinate populations against pneumococcal disease. The formulation required a preservative that met the antimicrobial effectiveness standards of the European Pharmacopoeia (EP), including deliberate multiple challenge studies, according to the recommendations in the WHO Open Vial Policy (41). The results of the study indicated that "2-PE provides a superior antimicrobial effectiveness over thimerosal…because thimerosal was not an effective preservative in reducing bioburden…and protecting multi-dose formulations against unintentional contamination in the field during multi-dose use of products that are kept at refrigerated temperatures," whereas 2-PE was stable, did not impact the stability of the vaccine and had a much higher rate of antimicrobial effectiveness in the vaccine formulations tested than those in which thimerosal was used (42).

Thus, the study demonstrated that 2-PE is *an effective preservative,* while thimerosal is either *a marginally effective or an ineffective preservative*. In terms of both cold-chain storage and multi-dose vials, the study showed that 2-PE is the superior, not the inferior, preservative for the safe preservation and distribution of the vaccine, regardless of where the vaccine might be sent. It is more effective and much safer when used as a preservative in multi-dose vials than is thimerosal, because it is neither as human-tissue toxic, nor as bioaccumulatively toxic as its Hg-based predecessor (43).

While the conclusion of the Pfizer study and other peer-reviewed scientific papers might have had an important impact at the INC negotiations were they well established in the minds of delegates, their import was lessened and even disputed by official submissions like those of the USA, which claimed that there was no alternative preservative comparable to thimerosal, even though 2-PE has been used in mandated vaccines given to American children for the past 70 years. In the face of opposite evaluations of thimerosal's effectiveness, safety and irreplaceability, one offered by NGOs and the other offered by public health authorities, INC delegates seemed ultimately to defer to the public health authorities.

Substituting thimerosal with 2-PE in vaccines for developing countries will require careful planning. The proponents of thimerosal specifically cite the regulatory process as the greatest obstacle to substitution, arguing that it is so cumbersome and costly that a ban on thimerosal will force the countries to use only single-dose vials (8). In a crisis situation, with an unsafe vaccine preservative being distributed to immunise around 84 million children in 120 countries every year, the regulatory process must be streamlined to permit the use of 2-PE in multi-dose vials in the developing nations as well as the developed nations, or to provide financial assistance to make a single-dose supply of vaccine available (8). With regard to the cost of switching to 2-PE at the manufacturing level, it has been estimated that the cost of a 0.5 mL dose of thimerosal in US$ in a 0.01% thimerosal-preserved vaccine is about $0.000441 and that of 2-PE in a 2.5% 2-PE-preserved vaccine is about $0.00228 (44). Thus, the apparent increase in cost would be $0.001839 per dose. However, this increase in cost would be offset by the reduced costs associated with handling, as well as the 2+% reduction in the amount of aqueous solution needed to be added to each vaccine vial. Thus, it may be concluded that the reduction in hazard would offset the minor increase in the per-dose cost of substituting thimerosal with 2-PE (44).

Most significantly, the cost of switching to a more effective and safer preservative must be weighed against the cumulative burden of avoidable harm being done to children by the thimerosal in their vaccines. If the Committee on Government

Reform of the US House of Representatives is correct in associating TCVs with autism (15), then the cost of maintaining thimerosal in the vaccine supply, unacknowledged by public health authorities, may be as high as $3.2 million per affected child over the course of his/her lifetime (45). This is an even more alarming figure when one considers the current rate of autism in the US is 1 in 68, a statistic derived from the early 2000s when the routine US vaccine schedule for children under 2 years of age could contain as much as 275 µg micrograms Hg from Thimerosal. Which developing nation would willingly incur this risk associated with TCVs in the independent scientific literature, when not only the intellectual, but also the economic cost and scale of harm is so great?

Along with NGOs, the United Methodist Women (UMW), a global organisation of women who advocate for the health and well-being of all, especially of women and children, described the presence of thimerosal in vaccines not as a financial but an ethical issue. In keeping with the historical global resolution of the United Methodist Church, "Protecting children from mercury-containing drugs," passed in 2008, the Deputy General Secretary of the UMW, Harriett Jane Olson, joined Rev Lisa K Sykes, the President of CoMeD, in expressing concerns about the ongoing use of TCVs to the INC. They stated: "In an era when cost-effective, much less toxic, non-bioaccumulative and more effective alternatives are available and in use as in-process sanitisers and preservatives, there is no conscionable justification for the continuing presence of thimerosal in human pharmaceuticals. We reject the notion offered by those who defend mercury in medicine that vaccine safety is static, and that, even though a safer global vaccine supply can be achieved by the removal of mercury from the manufacturing process, this inconvenience is somehow an undue burden especially when compared to sparing many children around the world from premature death or a lifetime of disability" (46).

In the light of the preceding statement, providing no-thimerosal and reduced-thimerosal vaccines to all, including the most vulnerable, be they children or nations and, thereby, protecting them from the avoidable risk of harm posed by TCVs, becomes a human rights issue.

Is it justice or discrimination to provide LMICs with Hg-containing vaccines?

Inexplicably, those championing a global Hg-free vaccine supply are not the agencies and industries which are responsible and liable for the global manufacture, approval and distribution of Hg-containing vaccines, but instead, only bellwether advocacy and faith-based organisations that have devoted themselves to championing the cause of the most vulnerable. Had those with immense power in the INC negotiations, especially WHO, acknowledged the danger posed by TCVs rather than disputing it, thimerosal-containing vaccines might not have been exempted from regulation in the Minamata Convention on Hg. Rather than the WHO and HICs, it was only "(t)wo US (NGOs who) pushed for the convention to phase out or phase down thimerosal, contending that it poses a risk to children's health. Numerous global health agencies led by the World Health Organization rallied to protect it, however, arguing that the preservative is safe and essential to vaccination programs that protect the world's poorest children from life-threatening diseases. A number of developing nations expressed concern about thimerosal during the negotiations, but in the end they supported its continued use, and the convention specifically exempts it" (47). Why would WHO, charged with protecting health worldwide, choose to protect the use of thimerosal in vaccines rather than protect developing children and nations from it? A history of critical statements made by WHO which illustrates its institutional intransigence regarding TCVs will now be presented for consideration.

The statements made by those holding national and global responsibility for vaccine safety are difficult to reconcile with the known and documented toxicity of thimerosal and ethyl-Hg compounds. For example, Francois et al from WHO and the US CDC stated in 2005, "Thimerosal (or thiomersal) has been used for a long time as an effective preservative in some vaccines, and a number of pharmaceutical and cosmetic products… Thimerosal has been used for >60 years in infant vaccines and other applications and has not been associated with adverse health effects in the general population… Hence, there is no reason to stop the use of thimerosal-containing vaccines in the current immunization programs worldwide. The balance of risks and benefits of these vaccines is very clearly positive" (48).

Years before the Minamata Convention on Hg was held, amid growing concerns about the safety of TCVs in the USA, Dr John Clements of WHO offered an emotional and subjective defence of thimerosal at a meeting of vaccine manufacturers, US government officials and others in Norcross, Georgia in 2000. This foreshadowed the prejudicial defence of TCVs that would be made by WHO to the INC. In Georgia, responding to the preliminary findings of a study that demonstrated the harm done by TCVs, Dr Clements stated [emphasis added], "I am really concerned that we have taken off like a boat going down one arm of the mangrove swamp at high speed, when in fact there was not enough discussion really early on about which way the boat should go at all. *And I really do want to risk offending everyone in the room by saying that perhaps this study should not have been done at all, because the outcome of it could have to some extent, been predicted***,** and we have all reached this point now where we are left hanging ... there is now the point at which the research results have to be handled, and even if this committee decides that there is no association (between TCVs and adverse events resulting from their administration) and that information gets out, the work that has been done and through the freedom of information that will be taken by others and will be used in ways beyond the control of this group. And I am very concerned about that as I suspect it is already too late to do anything regardless of any professional body and what they say. *My mandate as I sit here in the group is to make sure at the end of the day that 100,000,000 are immunized with DTP, Hepatitis B and if possible Hib, this year,*

next year and for many years to come, and that will have to be with thimerosal-containing vaccines..." (49).

On May 21, 2002, at a time when the thimerosal content in US vaccines was being phased out, a "WHO informal meeting on removal of thiomersal from vaccines and its implications for global vaccine supply" was held at the WHO headquarters in Geneva, Switzerland. A document released at that meeting stated [emphasis added]: "As part of a number of other activities, WHO organized a meeting with manufacturers that supply vaccines to the United Nations agencies in order to achieve a better understanding of the different approaches taken by manufacturers, to discuss the implications of the current WHO policy on keeping thiomersal in multi-dose vial presentations and to consider the implications of different actions for manufacturers. The group considered *two possible scenarios: to take thiomersal out of vaccines or keep it in***"** (50). Disturbingly, the document said, "WHO is concerned about the current situation whereby manufacturers in developed countries have been forced to lower thiomersal content of their vaccines..." Finally, the notes in this document indicated the following WHO strategies [emphasis added]: "On analysis of the pros and the cons of the various alternatives, the group considered that the best option would be *to maintain acceptance of thiomersal in vaccines for the global market*" (50).

The obdurate support of WHO for the continuing use of TCVs and for TCV manufacturers was also apparent in "Manufacturer perspectives on alternatives to thiomersal," a WHO informal consultation which was aimed at developing further guidance on vaccines for the UNEP-convened INC4, and which had input from Sanofi Pasteur, Novartis and Crucell (51). The presentation suggested that thimerosal is safe and is not associated with neurodevelopmental disorders, on the basis of epidemiological population studies, even though clinical and not epidemiological studies are required to prove the safety of a drug. In the presentation, the manufacturers suggested that "a suitable alternative (to thimerosal) may never be found," failing to recognise that one alternative, 2-PE, has become the acceptable, safer choice of the HICs. Having questioned even the possibility of switching to a safer, much less toxic preservative for the LMICs, the vaccine manufacturers then stated: "We recommend a long-term WHO policy on thiomersal use which defines a realistic timing for future request of switching." With a recurring focus on the "need to recover investments" should thimerosal be eliminated from vaccines (for LMICs), the manufacturers suggested that the development window for these formulations may be at least 7– 10 years away for LMICs (51).

Was a false dichotomy created by those who presented the issue in terms of a choice between TCVs or no vaccine at all, in the context of the developing countries, at the Minamata Convention on Hg? Was this dichotomy created through the exercise of undue influence by those most liable for the distribution of TCVs and the harm caused by them, upon those most susceptible to this exposure, with the help of incomplete and sometimes misleading information at global diplomatic negotiations? While vaccine manufacturers such as Merck affirmed that, "The role of the pharmaceutical industry in respecting and promoting health as a human right is complex. We believe that our most basic role is our core activity of discovering, developing and delivering medicines and vaccines to address unmet medical needs…We also recognize our ethical duty to support governments in their efforts to protect the right to health by 'doing no harm'" (52), the industry, without any incentive to make Hg-free the standard for vaccine formualtions, seems either unable or unwilling to recognize the public health crisis posed by Thimerosal in vaccines.

The extraordinary effort of WHO representatives to maintain thimerosal in the global vaccine supply, particularly for distribution to LMICs, would also seem to be in contradiction to the description of Dr Margaret Chan, Director-General, WHO, of the role of WHO: "(T)he world needs a global health guardian, a custodian of values, a protector and defender of health, including the right to health." In fact, in 2000, the UN Committee on Economic, Social and Cultural Rights adopted a General Comment on the Right to Health which defined its four essential elements as availability, accessibility, acceptability and quality. With respect to the Right to Health, WHO describes how it "has been actively strengthening its role in providing … political leadership on the right to health, including advocating for health-related human rights, including the right to health" (53).

The record of WHO on the issue of TCVs would seem to violate this right to health completely. As defined in the context of the right to health, quality means that "health facilities, goods and services must be scientifically and medically appropriate and of good quality." The responsibility upon State Parties abiding by the right to health includes the obligation "not to interfere with the enjoyment of the right to health ('do no harm')." How can WHO violate one of the elements of the right to health to which it requires State Parties to conform? Is thimerosal being maintained in the global vaccine supply because it is impossible to make the world's vaccine supply Hg-free, or because it is in the interests of TCV distributors not to let the benefits (lack of harm) of a global Hg-free vaccine supply become apparent? Given the independent published scientific literature (whether clinical, historical or epidemiological), all of which demonstrates that TCVs are associated with serious adverse events in some children, why would WHO, guild organisations (such as the AAP) and HICs (such as the USA) stubbornly defend the continuation of a known neurotoxin in the global vaccine supply?

Are vaccines, or the children to whom the vaccines are administered, being protected?

The global use of vaccines to eradicate diseases reflects the power and legitimacy of public health institutions and public health policies at every level of government. Vaccines are one of the single greatest advancements in medicine (54) and the cornerstone of public health policy, besides being a great source of revenue (55). However, their acceptance and the

acceptance of the authority that mandates them depend on the guarantee of their safety and efficacy. If millions of children are harmed by the use of an untested and toxic preservative in mandated vaccines, not only is the legitimacy of the vaccine programme called into question, but also the legitimacy of those who run the programme, and the vaccines themselves.

The discomfort created by the two conflicting ideas that (i) Hg is highly toxic even at low levels and may have significant adverse neurodevelopmental consequences in animal and human systems, and (ii) all mandated vaccines, including those containing Hg, are safe and effective, may be seen in terms of cognitive dissonance. According to the theory of cognitive dissonance, an individual faced with discomfort caused by the dissonance between two conflicting ideas will seek to reduce it. One way of doing this, described "in simple terms, can be the filtering of information that conflicts with what you already believe, in an effort to ignore that information and reinforce your beliefs" (56). Applying the theory of cognitive dissonance to the thimerosal controversy, the mantra that all vaccines are safe and effective may cause public health officials, institutions and researchers to contend that thimerosal is safe, despite the great amount of evidence to the contrary; the belief in the safety of vaccines is so non-negotiable in the estimation of WHO and other public health authorities that credible challenges to it, as in the case of the toxicity of thimerosal, must be dismissed.

Using the theory of cognitive dissonance to describe institutional corruption, Cosgrove and Whitaker reported: "Financial conflicts, whether arising from payments by a third party (such as a pharmaceutical company), or from guild interests, can lead researchers to engage in distorted science… and to develop imbalanced conclusions about the risk/benefit ratio of a class of medications..." (57) Such distorted research obscured the danger of another toxin, lead, the use of which was once deemed safe and beneficial in many marketed products (gasoline, paint and pipes). According to Bridbord and Hanson, the lead "industry was to use their public relations capabilities to advertise the benefits of their products to the general public while casting doubt on the possibility of harm associated with use of these products.… The lead industry was able to achieve its influence in large part by being the primary supporter of research on health effects of lead and relying upon the scientists that it supported to communicate and interpret this research to the government and the public" (58). Is this troubling paradigm of protecting the toxin rather than the public, and especially the children exposed to it, repeating itself? Furthermore, are vaccines immune to such corruption because they are life-saving medicines, or ironically are they uniquely susceptible to it, because a landmark reform in their manufacture might suggest a previous and significant lack of safety in a product mandated for administration because it is declared to be safe, effective and life-saving?

Applying the analysis of how the response to cognitive dissonance can corrupt and weaken a system, described by Cosgrove and Whitaker, (57) one may wonder whether the acceptance of thimerosal in some vaccine formulations intended for LMICs could be "the consequence of an influence within an economy of influence that illegitimately weakens the effectiveness of an institution, especially by weakening the public trust of the institution." Could the AAP's abrupt reversal in position on the safety of thimerosal, its fear of being perceived of as "asleep at the switch" by the US FDA with regard to thimerosal, and the statement by the US Committee on Government Reform that "our public health agencies' failure to act is indicative of institutional malfeasance for self-protection and misplaced protectionism of the pharmaceutical industry" (15) all be indications of an influence that has illegitimately weakened the effectiveness of the global vaccine programme, especially by weakening the public's trust in WHO and in the Minamata Convention on Hg, which was strongly influenced by WHO?

How will developing nations, left unprotected by the Minamata Convention on Hg, protect themselves from thimerosal?

Challenging WHO's defence of the use of TCVs in the developing nations, Cristina Girardi, a Deputy Minister in the Chilean Congress, declared while addressing INC4, "It is categorically unacceptable that the presence of this compound is recommended mostly for developing nations, which makes us question the seriousness of our international health authorities and their respect for the human rights of those who were born in the poorer geographical areas of the world" (59). Keeping in mind one of the essential elements of the right to health, acceptability, as defined by the UN, "All health facilities, goods and services must be respectful of medical ethics...as well as being designed to…improve the health status of those concerned" (10), nations must now act independently of the flawed diplomatic instrument emerging as the Minamata Convention on Hg and of the influences that produced it. They must press for national bans on TCVs to protect themselves and their citizens. The injustice of the two-tier system of vaccine safety sanctioned by the Convention should spur the developing nations to gain autonomy and expertise in the assessment and surveillance of public health policy and instruments. The evaluations made can then prompt legislation which would ensure sound acceptable standards in the areas of imported health products and practices. Above all else, these standards, products and practices should be in the best interest of the nation and free from discrimination.

A mere three months after the adoption of the Minamata Convention on Hg, Chile became the first developing nation to pass legislation aimed at banning thimerosal in vaccines (60). By doing so, this nation has sought to afford itself the protection from TCVs which the Convention denied it. Parents who knew that their children had been injured by TCVs, together with supportive elected government officials, led a successful campaign which, on January 15, 2014, resulted in the passage of national legislation that eliminated anything more than a trace level of thimerosal in vaccines. This was achieved in the face of opposition from global public

Table 1
The thimerosal content of various types of vaccines in different countries

General vaccine type	Country group [HIC or LMIC]	Specific vaccine [brand name]*	Manufacturer*	Mercury content from thimerosal
Pertussis-containing vaccines	HIC	DTaP [Infanrix]	GSK	0 µg/dose
		DTaP [Tripedia]	Sanofi Pasteur, Inc	≤ 0.3 µg/dose
	LMIC	DTwP-HepB [Tritanrix HepB]	GSK	12.5 µg/dose
		DTwP [DT COQ]	Sanofi Pasteur SA	25 µg/dose
Diphtheria–tetanus vaccines	HIC	DT [none]	Sanofi Pasteur, Inc	< 0.3 µg/dose
	LMIC	DT [none]	Sanofi Pasteur SA	25 µg/dose
Hepatitis B vaccines	HIC	HepB [Recombivax HB]	Merck	0 µg/dose
		HepB [Engerix B]	GSK	0 µg/dose
	LMIC	HepB [Shanvac-B]	Shanta Biotechnics Pvt Ltd	25 µg/dose
		HepB [Heber Biovac HB]	Laboratorio Bago de Chile SA	12.5 µg/dose
		HepB [none]	Laboratorio Volta SA	12.5 µg/dose
		HepB [none]	Laboratorios D & M Pharma Ltda	12.5 µg/dose
		HepB [none]	Merck	12.5 µg/dose
Meningococcal meningitis vaccines	HIC	*N. meningitidis* [Menactra]	Sanofi Pasteur, Inc	0 µg/dose
	LMIC	*N. meningitidis* [VA-Mengoc-BC]	Laboratorios Lafi Ltda	25 µg/dose

**GSK: GlaxoSmithKline Biologicals; DT: diphtheria and tetanus; DTaP: diphtheria, tetanus and acellular pertussis; DTwP: diphtheria, tetanus and whole-cell pertussis; HepB: hepatitis B; HIC: high-income country; LMIC: low- and middle-income country; and µg: microgram.*

health organisations, including the Pan American Health Organization. The law, now awaiting the signature of Chile's president, has the following provision: "Thimerosal will be banned from all vaccines for the most vulnerable segments of the population (children 0–8 years of age, pregnant women, and adults over 60 years of age)" (60). If signed by the president, the law will take effect six months later. Clearly, the passage of this law, whether or not it is ultimately signed by the president, demonstrates that the people of Chile are challenging the exemption of TCVs by the Minamata Convention on Hg and the legitimacy of WHO.

The assertions that thimerosal is safe, even for pregnant women and developing children in LMICs, by public health institutions and powerful government agencies in HICs responsible for shaping global vaccine policy seem to be characterised by a desire to reduce cognitive dissonance. Now, developing nations which wish to protect their children from the avoidable risk posed by thimerosal must follow Chile's example, challenging the influence and assurances of WHO and the legitimacy of the Minamata Convention on Hg. The current situation, in which TCVs are disproportionately distributed to developing nations, is unethical and must be remedied by the introduction of a single global standard of vaccine safety (no-thimerosal/reduced-thimerosal) for all persons, if the legacy of this diplomatic instrument and of the vaccine programme led by WHO is to be remembered as one of achievement rather than discrimination.

Conclusion

On October 10, 2013, in Kumamoto, Japan, the nations represented in the INC of the UNEP adopted the Minamata Convention on Hg. While their efforts to eliminate and reduce some forms of exposure to Hg are laudable, the specific exemption of the Hg-based compound thimerosal, used as a preservative in certain vaccines, from regulation has given rise to the discriminatory practice of providing TCVs to LMICs and no-thimerosal and reduced-thimerosal vaccines to HICs. While thimerosal is a poison that affects all systems in the body, it affects some physiological systems more than others and accumulates in some target organs more than others. Similarly, due to the Minamata Convention on Hg and the exemption of TCVs from regulation, and thus, their inequitable but sanctioned distribution, thimerosal is also adversely affecting some parts of the world more than others and accumulating in some targeted nations much more than others. This historic failure of diplomatic policy is in direct conflict with the right to health, as affirmed by the UN and WHO. The continuing distribution of TCVs to the LMICs was defended during the negotiations by the HICs, which have removed thimerosal from their own vaccine supplies, by guild organisations such as the AAP, the membership of which is responsible for administering TCVs, and by WHO, which continues to provide TCVs to the LMICs. The rationale for continuing the distribution of TCVs to the LMICs was that thimerosal is essential, safe and effective – claims that have been shown to be untrue. Public health policy leaders must consider whether the denial of the risk posed by TCVs is the consequence of a systemic response to the phenomenon of cognitive dissonance, resulting in the unassailable conclusion that all vaccines, even TCVs, are safe and effective despite the absence of evidence to support this conclusion. What is at stake is public confidence in the global vaccination programme and the well-being of children. Much safer, economic and less toxic alternatives, such as 2-PE, can replace thimerosal in preserved multi-dose vaccines intended for the LMICs. The global vaccine supply must be made Hg-free, and there should be a unified and high standard of vaccine safety for all persons, regardless of the wealth possessed by their country of origin. In a hundred years, others will evaluate whether the good accomplished by the Minamata Convention on Hg outweighed the injustice that it perpetrated by exempting TCVs from regulation, resulting in their disproportionate distribution to the most vulnerable among us – developing children in developing nations.

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Commentary

Controversies surrounding mercury in vaccines: autism denial as impediment to universal immunisation

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In 2004, the US Center for Disease Control (CDC) published a paper showing that there is no link between the age at which a child is vaccinated with MMR and the vaccinated children's risk of a subsequent diagnosis of autism (1). One of the authors, William Thompson, has now revealed that statistically significant information was deliberately omitted from the paper (2). Thompson first told Dr S Hooker, a researcher on autism, about the manipulation of the data. Hooker analysed the raw data from the CDC study afresh. He confirmed that the risk of autism among African American children vaccinated before the age of 2 years was 340% that of those vaccinated later. Hooker published his findings in the peer-reviewed open-access journal, *Translational Neurodegeneration*. However, within hours of CNN publishing the story of the CDC whistle-blower, Hooker's article was removed from the website of the open-access journal. It was stated that the journal and publisher "believe that its continued availability may not be in the public interest". The full article is now available only on the PubMed website (3).

The MMR vaccine contains no Thimerosal, but the story of Thompson and the paper on MMR serves to illustrate how disputed the areas of vaccine-related injury and autism have become.

Protection from mercury as an equity issue

This issue of the *IJME* features an article by Sykes and colleagues on Thimerosal – a mercury-based preservative used in vaccines (4). The article inveighs against the exemption under the UN Convention on Mercury (Minamata Convention) that allows the use of Thimerosal-containing vaccines in developing countries. The authors, who are from the Coalition for Mercury-free Drugs and the Institute of Chronic Illnesses, argue that developing children and developing nations are the most vulnerable to toxic exposures and the UN's primary aim should be to protect them. They sidestep contentious issues, such as claims about vaccine-related injury, and dwell mainly on the matter of unfair discrimination.

The demand for mercury-free vaccines, however, springs from the perception that the heavy metal added to vaccines is harmful. It is felt that there was a spike in the incidence of autism in the USA when the *Haemophilus influenza b* (Hib) and hepatitis B vaccines were recommended for universal use (5). This commentary attempts to bring together the evidence. We discuss the need for mercury in vaccines and the suggestion that the use of ethyl mercury is safe. It draws extensively on a US House of Representatives report, "Mercury in Medicine Report" (6).

Thimerosal as preservative in vaccines

Thimerosal is an organic mercurial compound made up of equal parts of thiosalicylic acid and ethyl mercury. Ethyl mercury dissociates from Thimerosal and acts as a preservative (7). Thimerosal is used to prevent bacterial contamination of vials which are entered multiple times, ie multi-dose vials of vaccines. Preservatives are not required for single-dose ampoules.

Methyl mercury experience

Thimerosal has been in use since the 1930s in a number of biological and drug products (8). The US Food and Drug