From the Preamble of the Proposed Power Plant Mercury and Air Toxics Standards

a. Overview of Hg and Associated Health and Environmental Hazards

Mercury is a persistent, bioaccumulative toxic metal that is emitted from EGUs in three forms: gaseous elemental Hg (Hg^0), oxidized Hg compounds (Hg^{+2}), and particle-bound Hg (Hg_P). Elemental Hg does not quickly deposit or chemically react in the atmosphere, resulting in residence times that are long enough to contribute to global scale deposition. Oxidized Hg and Hg_P deposit quickly from the atmosphere impacting local and regional areas in proximity to sources. Methylmercury is formed by microbial action in the top layers of sediment and soils, after Hg has precipitated from the air and deposited into waterbodies or land. Once formed, MeHg is taken up by aquatic organisms and bioaccumulates up the aquatic food web. Larger predatory fish may have MeHg concentrations many times, typically on the order of one million times, that of the concentrations in the freshwater body in which they live. Although Hg is toxic to humans when it is inhaled or ingested, we focus in this rulemaking on exposure to MeHg through ingestion of fish, as it is the primary route for human exposures in the U.S., and potential health risks do not likely result from Hg inhalation

exposures associated with Hg emissions from utilities.

In 2000, the National Research Council (NRC) of the NAS issued the NAS Study, which provides a thorough review of the effects of MeHg on human health. There are numerous studies that have been published more recently that report effects on neurologic and other endpoints.

i. Reference and Benchmark Doses

As discussed earlier in Sections II.A.1 and III.B.3.a.i of this preamble, EPA has set and evaluated the RfD for Hg several times, and has received input from the NRC on the appropriateness of the RfD. In 1995, EPA set a health-based ingestion rate for chronic oral exposure to MeHg termed an oral RfD, at 0.0001 milligrams per kilogram per day (mg/kg-day).[1] The RfD was based on effects reported for children exposed *in utero* during the Iraqi Hg poisoning episode, in which children were exposed to high levels of Hg when their mothers consumed contaminated grain.[2] Subsequent research from large epidemiological studies in the Seychelles,[3] Faroe Islands,[4] and

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[1] MeHg exposure is measured as milligrams of MeHg per kilogram of bodyweight per day, thus normalizing for the size of fish meals and the differences in bodyweight among exposed individuals.

[2] Marsh DO, Clarkson TW, Cox C, Myers GJ, Amin-Zaki L, Al-Tikriti S 1987. Fetal methylmercury poisoning. Relationship between concentration in single strands of maternal hair and child effects. Arch Neurol 44(10):1017–1022.

[3] Davidson, P.W., G. Myers, C.C. Cox, C.F. Shamlaye, D.O.Marsh, M.A.Tanner, M. Berlin, J. Sloane-Reeves, E. Chernichiari, , O.

New Zealand[5] added substantially to the body of knowledge on neurological effects from MeHg exposure. In 2001 EPA established a revised RfD based on the advice of the NAS and an independent review panel convened as part of the Integrated Risk Information System (IRIS) process. In their analysis, the NAS examined in detail the epidemiological data from the Seychelles, the Faroe Islands, and New Zealand, as well as other toxicological data on MeHg. The NAS recommended that neurobehavioral deficits as measured in several different tests among these studies be used as the basis for the RfD.

The NAS proposed that the Faroe Islands cohort was the most appropriate study for defining an RfD, and specifically selected children's performance on the Boston Naming Test (a neurobehavioral test) as the key endpoint. Results from all three studies were considered in defining the RfD, as published in the "2001 Water Quality for the Protection of Human Health:

Choisy, A. Choi and T.W. Clarkson. 1995. Longitudinal neurodevelopment study of Seychellois children following in utero exposure to methylemrcury form maternal fish ingestion: outcomes at 19 and 29 months. NeuroToxicology 16:677-688.

[4] Grandjean, P., Weihe, P., White, R.F., Debes, F., Araki, S., Murata, K., Sørensen, N., Dahl, D., Yokoyama, K., Jørgensen, P.J., 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol. Teratol. 19, 417–428.

[5] Kjellstrom T, Kennedy P, Wallis S, Stewart A, Friberg L, Lind B, et al. (1989). Physical and mental development of children with prenatal exposure to mercury from fish. Stage 2: Interviews and psychological tests at age 6. Solna, Sweden: National Swedish Environmental Protection Board. Report No.: Report 3642.

Methylmercury," and in the IRIS summary for MeHg: "Rather than choose a single measure for the RfD critical endpoint, EPA based this RfD for this assessment on several scores from the Faroes' measures, with supporting analyses from the New Zealand study, and the integrative analysis of all three studies."[6]

EPA defined the updated RfD of 0.0001 mg/kg-day in 2001. Although derived from a more complete data set and with a somewhat different methodology, the current RfD is numerically the same as the previous (1995) RfD (0.0001 mg/kg-day, or 0.1 µg/kg-day).

This RfD, consistent with the standard definition, is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (EPA, 2002). In general EPA believes that exposures at or below the RfD are unlikely to be associated with appreciable risk of deleterious effects. However, no RfD defines an exposure level corresponding to zero risk; moreover the RfD does not represent a bright line, above which individuals are at risk of adverse effects. EPA's interpretation for this assessment is that any exposures to MeHg above the RfD are of concern given the nature of the data available for Hg that is not necessarily available

[6] EPA, 2001

for many other chemicals. The scientific basis for the Hg RfD includes extensive human data and extensive data on sensitive subpopulations, including pregnant mothers; therefore, the RfD does not include extrapolations from animals to humans, and from the general population to sensitive subpopulations. In addition, there was no evidence of a threshold for MeHg-related neurotoxicity within the range of exposures in the Faroe Islands study which served as the primary basis for the RfD. This additional confidence in the basis for the RfD suggests that all exposures above the RfD can be interpreted with more confidence as causing a potential hazard to public health. Studies published since the current MeHg RfD was released include new analyses of children’s neuropsychological effects from the existing Seychelles and Faroe Islands cohorts, including formation of a new cohort in the Faroe Islands study. There are also a number of new studies that were conducted in population-based cohorts in the U.S and other countries. A comprehensive assessment of the new literature has not been completed by EPA. However, data published since 2001 are generally consistent with those of the earlier studies that were the basis of the RfD, demonstrating persistent effects in the Faroe Island cohort, and in some cases associations of effects with lower MeHg exposure concentrations than in the Faroes. These new studies provide additional confidence that exposures above the RfD are

contributing to risk of adverse effects, and that reductions in exposures above the RfD can lead to incremental reductions in risk.

ii. Neurologic Effects

In its review of the literature, the NAS found neurodevelopmental effects to be the most sensitive and best documented endpoints and appropriate for establishing an RfD;[7] in particular NAS supported the use of results from neurobehavioral or neuropsychological tests. The NAS report[8] noted that studies in animals reported sensory effects as well as effects on brain development and memory functions and support the conclusions based on epidemiology studies. The NAS noted that their recommended endpoints for an RfD are associated with the ability of children to learn and to succeed in school. They concluded the following: "The population at highest risk is the children of women who consumed large amounts of fish and seafood during pregnancy. The committee concludes that the risk to that population is likely to be sufficient to result in an increase in the number of children who have to struggle to keep up in school."

iii. Cardiovascular Impacts

The NAS summarized data on cardiovascular effects available

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[7] NAS, 2000
[8] NAS, 2000

up to 2000 (IRIS 2001). Based on these and other studies, the NRC (2000) concluded that “Although the data base is not as extensive for cardiovascular effects as it is for other end points (i.e., neurologic effects) the cardiovascular system appears to be a target for MeHg toxicity in humans and animals.” The NRC also stated that “additional studies are needed to better characterize the effect of methylmercury exposure on blood pressure and cardiovascular function at various stages of life.”

Additional cardiovascular studies have been published since 2000. EPA did not to develop a quantitative dose-response assessment for cardiovascular effects associated with MeHg exposures, as there is no consensus among scientists on the dose-response functions for these effects. In addition, there is inconsistency among available studies as to the association between MeHg exposure and various cardiovascular system effects. The pharmacokinetics of some of the exposure measures (such as toenail Hg levels) are not well understood. The studies have not yet received the review and scrutiny of the more well-established neurotoxicity data base.

iv. Genotoxic Effects

The Mercury Study noted that MeHg is not a potent mutagen but is capable of causing chromosomal damage in a number of experimental systems. The NAS concluded that evidence that

human exposure to MeHg caused genetic damage is inconclusive; they note that some earlier studies showing chromosomal damage in lymphocytes may not have controlled sufficiently for potential confounders. One study of adults living in the Tapajós River region in Brazil[9] reported a direct relationship between MeHg concentration in hair and DNA damage in lymphocytes; as well as effects on chromosomes. Long-term MeHg exposures in this population were believed to occur through consumption of fish, suggesting that genotoxic effects (largely chromosomal aberrations) may result from dietary, chronic MeHg exposures similar to and above those seen in the Faroes and Seychelles populations.

v. Immunotoxic Effects

Although exposure to some forms of Hg can result in a decrease in immune activity or an autoimmune response,[10] evidence for immunotoxic effects of MeHg is limited.[11]

vi. Other Human Toxicity Data

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[9] Amorim, M.I., Mergler, D., Bahia, M.O., Dubeau, H., Miranda, D., Lebel, J., Burbano, R.R., Lucotte, M., 2000. Cytogenetic damage related to low levels of methyl mercury contamination in the Brazilian Amazon. An. Acad. Bras. Cienc. 72, 487–507.

[10] Agency for Toxic Substances and Disease Registry (ATSDR). 1999. Toxicological profile for Mercury. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service. http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=115&tid=24.

[11] National Academy of Sciences. Toxicologic effects of methylmercury. Washington, DC: National Research Council, 2000. Available online at http://www.nap.edu/openbook.php?isbn=0309071402.

Based on limited human and animal data, MeHg is classified as a “possible” human carcinogen by the International Agency for Research on Cancer (IARC)[12] and in IRIS.[13] The existing evidence supporting the possibility of carcinogenic effects in humans from low-dose chronic exposures is tenuous. Multiple human epidemiological studies have found no significant association between Hg exposure and overall cancer incidence, although a few studies have shown an association between Hg exposure and specific types of cancer incidence (e.g., acute leukemia and liver cancer[14]).

There is also some evidence of reproductive and renal toxicity in humans from MeHg exposure. However, overall, human data regarding reproductive, renal, and hematological toxicity from MeHg are very limited and are based on either studies of the two high-dose poisoning episodes in Iraq and Japan or animal data, rather than epidemiological studies of chronic exposures at the levels of interest in this analysis.

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[12] IARC, 1994
[13] EPA, 2002
[14] NAS, 2000