Mr. Chairman and distinguished members of the Committee—I am pleased to appear before you today to present testimony on our current understanding regarding chemical contaminants in drinking water. My name is Linda Birnbaum; I am the Director of the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health and Director of the National Toxicology Program (NTP).

NIEHS and NTP have funded years of research on hazardous chemicals in the environment that can affect human health, including chemicals that are sometimes found as contaminants in drinking water. I will address three specific contaminants of interest: hexavalent chromium, perchlorate, and trichloroethylene.

**Hexavalent chromium**, or chromium VI, is a form of chromium that is produced and used in many industrial processes, such as electroplating, stainless steel production, leather tanning, textile manufacturing, and wood preservation. Many people know of it as the chemical contaminant featured in the movie, “Erin Brockovich”. This chemical is listed in the NTP’s Report on Carcinogens as a *known human carcinogen*; it was first listed in 1980.¹ The chromium molecule exists mostly in either trivalent (chromium III) or hexavalent (chromium VI) states. Chromium III is an essential micronutrient at low doses, although it can be toxic in large doses; chromium VI is about a thousand times more toxic than chromium III.²

It is well established that ingestion of high concentrations of hexavalent chromium can lead to severe gastrointestinal distress and death. Review of unfortunate accidental exposures and suicides indicates an acute lethal concentration as low as 4.1 milligrams of hexavalent chromium per kilogram body weight.³ Long term exposures of workers to hexavalent chromium on the

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skin have been shown to cause severe skin lesions and irritation. However, these effects are not expected at the very much lower doses associated with most people’s exposure from public drinking water.

When inhaled, chromium VI is genotoxic to humans, meaning that it can damage DNA through the production of reactive oxygen. The carcinogenic effects of breathing chromium VI (nasal, sinus, and lung cancer) are well established. However, for a long time, this genotoxic mechanism and resultant carcinogenicity from inhalation were not so clear for the case where it is ingested, as in drinking water. NTP has done extensive animal testing to provide information on chromium VI toxicity and carcinogenicity via drinking water. The NTP studies showed that sodium dichromate dihydrate, a water-soluble salt of chromium VI, caused cancer in laboratory animals following oral ingestion in drinking water.

NIEHS-funded researchers are continuing work on chromium VI. Investigators at New York University have been looking at mechanisms of ingested chromium VI toxicity, exploring the ways in which it may affect epigenetic programming and gene silencing and ultimately lead to cancer. Another research group at Brown University is studying the mechanism of DNA-chromium VI adduct formation and DNA-protein crosslinking by chromium VI using in vitro models. They have suggested that the DNA modifications produced by chromium VI in human cells could serve as highly specific indicators of individual dose. A separate study in a rat model is looking at whether lactational exposure to chromium VI affects ovarian development in offspring. Even more importantly, other NIEHS-funded researchers in our Superfund research program are developing new methods for removing chromium VI and other metals from water supplies.

**Perchlorate** is a chemical found naturally in arid climates and is manufactured in the U.S. for a variety of uses primarily as a solid rocket propellant (e.g., in munitions, flares and fireworks). In the past, perchlorate has been used in the treatment of human diseases and is still used as a diagnostic tool in medicine (the perchlorate discharge test, which is used to diagnose thyroid defects involving abnormal iodide processing). Perchlorate is of interest as a drinking water contaminant, because it can affect levels of thyroid hormones by inhibiting the transport of iodide into the thyroid. Inhibition of iodide uptake can disturb the normal production of thyroid hormones that play an essential role in fetal and post-natal neurodevelopment. These hormones also regulate neuropsychological development in children and adults. Usually, the body maintains normal production of thyroid hormones even in cases of iodide deficiency.

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7 Epigenetic programming refers to the ways in which nonsequence-related modifications of the DNA molecule regulate gene expression.
However, in pregnant women, severe iodide deficiency can result in adverse neurodevelopmental effects in the fetus and newborn. This raises the possibility that a similar outcome could be produced by exposure to perchlorate in drinking water at sufficient levels and for a sufficient period of time. However, to date, human studies on environmental exposure to low levels of perchlorate have been inconsistent. The authors of a 2005 National Research Council study, “Health Implications of Perchlorate Ingestion”, based their conclusions primarily on clinical data collected in controlled settings, particularly those described in an article by MA Greer and his colleagues. The NRC found the epidemiological studies in human populations to be limited with respect to this question. Further research is required to determine if there are effects on vulnerable groups such as low birth weight or preterm infants, or whether maternal perchlorate exposure (with or without low dietary iodide intake) causes neurodevelopmental outcomes in infants.

Information continues to be generated about these questions. A series of papers between 2009 and 2011 has confirmed that fetuses and infants demonstrate exposure to levels of perchlorate that are associated with maternal levels, albeit not with concentrations in their drinking water. A cross-sectional study of 1641 first trimester pregnant women (including 1002 pregnant women with low urinary iodide levels) found no relationship between urinary perchlorate and clinical measures of serum TSH and freeT4 (Pearce et al. 2010). In another report, perchlorate exposure was associated with increased urinary thyroid-stimulating hormone (TSH) in infants with low urinary iodide, although T4 levels were not reduced. In a recent ecological epidemiological study in California, researchers were able to show elevated TSH levels in infants from perchlorate-exposed communities (defined as drinking water levels greater than 5 micrograms/liter). The question of whether these hormone levels result in actual impacts on health and development is unknown and remains an important question for further research.

Development of new techniques for remediation is also important in this area. In a Small Business Innovative Research project, part of our Superfund Research Program, NIEHS is supporting a group that is working to transform a proof-of-concept prototype for an online

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15 http://www.nap.edu/openbook.php?record_id=11202&page=R1
perchlorate detection and remediation system. They will also develop a companion field portable prototype for water source spot analysis in the field.

**Trichloroethylene (TCE)** is a solvent that is widely used for degreasing and cleaning metals. TCE has many other industrial uses as an extraction solvent for organic oils, as a reactant in the production of other chemicals, and in the manufacturing of fluorocarbons. TCE is widely available as a household cleaner and is found as an ingredient in a number of consumer products such as adhesives, rug cleaning fluid, paint removers, spot removers, and typewriter correction fluid. Due to its widespread use throughout the U.S., TCE is often found as a contaminant in ground water and drinking water. Due to its volatility and low water solubility, TCE can readily evaporate from contaminated water posing an additional concern for inhalation exposure. This is particularly important in the enclosed space of the home where showering, dishwashing, and laundry activities can increase the potential for exposure by both inhalation and absorption through the skin.

TCE has been a contaminant of concern for decades. In a 1988 report, children exposed to a water supply that included TCE contamination, were reported to have experienced increased respiratory disease such as bronchitis, asthma and pneumonia. In this case, the wells supplying drinking water were contaminated with multiple solvents besides TCE, including a related chemical, tetrachloroethylene (also known as perchloroethylene or perc). As in this case, human epidemiological studies are often complicated by exposures to mixtures, making interpretation of the data difficult.

The link between exposure to TCE and cancer in humans is controversial due, in part, to such mixed chemical exposures. However, a statistically significant association between TCE exposure and increased incidence of leukemia among the highest group of exposed females was demonstrated in a study conducted in New Jersey. Again, this study was complicated by several uncertainties, including lack of detailed information about the magnitude of individual exposures and a poor understanding of the relative exposure contribution from inhalation and ingestion. A follow-up study of over 1.5 million residents in 75 different towns showed statistically significant elevations in total leukemias, child leukemia, acute lymphatic leukemia and non-Hodgkin’s lymphoma in groups of females exposed to TCE concentrations greater than 5 ppb. A more recent occupational study, published in 2007 and adjusting for multiple chemical exposures, showed associations between occupational exposures to TCE and prostate cancer.

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Following several controversial studies conducted in Woburn, MA, the Massachusetts Department of Health concluded that there was an 8-fold higher risk of leukemia in the group that was exposed in utero, and that this increase may be related to the exposure of mothers to solvent-contaminated drinking water during pregnancy. These studies, too, are complicated by mixed chemical exposures and uncertainties about the levels of exposure.

Trichloroethylene was listed in the NTP’s Report on Carcinogens as reasonably anticipated to be a human carcinogen based on limited evidence of carcinogenicity from seven studies in humans supported by evidence of carcinogenicity in experimental animals, in which tumors occurred at several of the same sites (especially liver) as in humans. A contemporary review of epidemiological literature showed that TCE was associated with excess incidences of liver cancer, kidney cancer, non-Hodgkin’s lymphoma, prostate cancer, and multiple myeloma, with the strongest evidence for the first three cancers. Nevertheless, as was noted at the time, these studies were based on a relatively small number of exposed workers and were confounded by exposure to other solvents and other risk factors.

More recent studies have been detailed in reviews appearing in the peer-reviewed literature in 2006 and 2008. Much information has emerged about the complexity of the biological effects of exposure to TCE. The understanding of metabolism of TCE has been critical to this process, because for many types of observed toxicity, the active agent or agents is actually a mixture of metabolites of the parent TCE compound, acting in concert with each other, with the parent, and with other co-contaminants typically encountered along with TCE such as tetrachloroethylene. More recent epidemiology provides further support for associations between TCE exposure and some level of excess risk of kidney cancer, liver cancer, and lymphomas, and to a lesser extent, cervical cancer and prostate cancer. However, scientists continue to debate the interpretation of these studies, considering such factors as different classifications of lymphomas, differences in data and methods for assigning TCE exposure status, and different statistical approaches.

NIEHS-funded work on TCE is continuing in several programs. The new Northeastern University Superfund Research Center grant is investigating drinking water as a possible source for chemical exposures (TCE, phthalates, and others) in Puerto Rico. This multidisciplinary project combines hydrogeological, epidemiological and mechanistic research on these and other chemicals to determine whether any are associated with risk of preterm birth. This Center is also...

32 Ibid
testing a new remediation strategy that utilizes solar energy as a means to break down TCE in groundwater. The University of Washington’s Superfund Research Center investigates a plant-based remediation strategy (phytoremediation) to break down organic chemicals such as TCE and tetrachloroethylene. Their innovative approach utilizes a poplar tree that has been genetically modified to express a mammalian gene (CYP2E1) that rapidly metabolizes TCE inside the plant. The University of Arizona is investigating the geological properties that determine movement of TCE and tetrachloroethylene underground and are applying their research at the Tucson International Airport Area (TIAA) Superfund complex. Understanding how these chemicals migrate and dissolve will aid in the removal or clean-up of these contaminants. The NIEHS Superfund program also funds new technologies for remediation of TCE contamination, such as the methods under development by a group at the University of Kentucky. They have pioneered a new type of nanoparticle filter that shows promise for the removal of TCE and other chemicals.

In conclusion, it is important to remember that determining risk from chemical exposures, through drinking water or through any other route of exposure, is a complex, nuanced enterprise. New data are telling us to consider not only dose, but timing of exposure, inherent susceptibility of the exposed individual, and effects of multiple types of exposures when determining risk from a particular chemical. Making these regulatory decisions is the responsibility of EPA and our other regulatory agency partners. At NIEHS, we are proud of the role we have played and continue to play in providing the best possible science to support this incredibly difficult task. We are committed to advancing the science to new heights, using the newest tools in the biomedical sciences to improve our understanding of the effects of environmental chemicals and to promote effective strategies for exposure reduction and disease prevention.

Thank you for the opportunity to testify. I will be happy to take your questions.

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