February 25, 2010

The Honorable Edward J. Markey
Chairman, Subcommittee on Energy and Environment
Committee on Energy and Commerce
United States House of Representatives
Washington, D.C. 20515

The Honorable Fred Upton
Ranking Member, Subcommittee on Energy and Environment
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Dear Chairman Markey and Ranking Member Upton:

The House Subcommittee on Energy and Environment is scheduled to hear testimony today from several witnesses concerning potential risks from "endocrine disruptors" in drinking water. The American Chemistry Council (ACC), a national trade association representing 140 member companies which employ 800,000 workers, requests that ACC's perspectives on this issue be entered into the hearing record.

In 1996, in response to public concern that some substances may interfere with endocrine processes in humans and wildlife, Congress directed the EPA, to develop a screening program, using appropriate validated test systems and other scientifically relevant information, for evaluating the potential of substances to induce hormone-related health effects. [1] The Food Quality Protection Act (FQPA) mandated the screening of pesticide chemicals and gave EPA authority to require screening of certain other substances. It also required EPA to "take action" as appropriate, on substances found to have an endocrine effect on humans, under existing statutory authority available to EPA. Shortly after passing the FQPA, Congress also passed an amendment to the Safe Drinking Water Act (SDWA) that gave EPA authority to test (in accordance with the FQPA provisions) for endocrine effects, substances that may be found in sources of drinking water if EPA determines that a substantial population may be exposed to such substance.[2]

After these laws were enacted, it quickly became apparent, as the result of a stakeholder advisory process conducted by EPA, that the scientific complexity of the endocrine system and the technical difficulties of screening and testing chemicals for endocrine disruption would be major challenges. EPA assessed the current state of the science and found that there were few, if any, scientifically valid screens and tests available to study the potential endocrine activity of chemical substances. Therefore EPA initiated an

[1] Food Quality Protection Act of 1996, 21 U.S.C. 346(a)-§408(p)
[2] Safe Drinking Water Act Amendments of 1996, 42 U.S.C. 300j-17

extensive research and development program, composed of both basic and applied research, to develop, standardize and validate the necessary endocrine test methods for its Endocrine Disruptor Screening Program (EDSP). The EPA has expended over $100 million dollars since 1996 on this joint applied- and basic-research effort.

The American Chemistry Council (ACC) has played a constructive role in the Agency's development of the EDSP. Our goals have been to see the EDSP implemented as quickly and efficiently as possible and in a manner consistent with the law, the science and ACC members' commitment to the safe manufacture, transport, use and disposal of chemicals. To those ends, ACC has consistently supported increased funding for the Agency's research and laboratory studies to develop, standardize and validate the screening and testing methods required for the EDSP. ACC also has sponsored technical studies to supply needed data for endocrine test development and validation, and has participated with the broader scientific and stakeholder communities on EPA's standardization and validation advisory committees. Further, ACC has sponsored scientific research on the endocrine hypothesis through its Long-Range Research Initiative.[3]

These actions demonstrate that with respect to endocrine disruption, as with any potential chemical risks, ACC members take these concerns seriously. We have committed substantial resources and expertise to make sure that there are well established scientifically robust methods for assessing endocrine activity and adverse effects, and that there are well established regulatory processes to act on this scientific information. Having confidence in the scientific information is critical, as this is the necessary foundation for assuring that chemicals and the products of chemistry are used safely and effectively.

A related key principle is that we must harness advances made in science and technology in our laws and regulations. Many emerging technologies like computational toxicology, molecular tools and computer modeling hold great promise for improving how we screen chemicals for endocrine activity. ACC very actively supports the development of these promising techniques. To date, however, they haven't been shown to meet the scientific standards of reliability, sensitivity and specificity. While some emerging technologies may be nearing the point of use, they are not there yet. But as new technologies are proposed to be integrated into EPA's endocrine screening program, they must be appropriately validated so that their results can be relied upon and replicated by different labs. They must be shown to measure what they purport to measure and do so with an acceptable degree of accuracy. Doing so will provide regulatory certainty and ensure protection of human health and the environment.

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[3] http://www.americanchemistry.com/s_acc/sec_lri.asp?CID=1369&DID=5053
http://www.americanchemistry.com/lrisearch/

The importance of basing regulatory decisions on the best science cannot be overstated. Decisions not based on the best science and on established risk assessment and management procedures can misallocate limited resources and limit the use of safe chemicals, and create potentially unnecessary public health concerns. In an attachment to this statement is a more in-depth discussion of three additional science topics that are important in your subcommittee's consideration of the endocrine issue in the context of the Safe Drinking Water Act. These topics address: a) mechanism of action and adverse effects; b) effects mediated by endocrine pathways that are addressed in outcomes from toxicity tests; and c) the "low dose" hypothesis. (See Attachment A.)

EPA has begun issuing endocrine test orders for certain pesticide chemicals and has also been charged by Congress to begin to identify certain drinking water contaminants for endocrine screening. ACC welcomes the opportunity to comment on the Agency's criteria for identifying drinking water contaminants for endocrine screening. We understand that if after screening and testing, EPA finds that certain substances pose adverse effects via endocrine mechanisms, EPA has existing authority to take actions to protect public health. This was the case in 1996 when Congress passed the endocrine screening requirements under the FQPA and the SDWA amendments, and is still the case today.

Finally, it is important to note that ACC supports improvements to the US chemical management framework to ensure the safety of chemicals in commerce today. To that end, ACC is on record calling for Congress to modernize the Toxic Substances Control Act, which is the primary federal law regulating chemicals in commerce, including chemicals that may be found in drinking water. I call your attention to ACC's principles for modernizing TSCA for your information.[4]

ACC and its members look forward to working with you and the entire Committee as discussions around the endocrine issue continues. If we can provide any additional information on ACC's perspectives on this or related topics, please contact me.

Sincerely,

Cal Dooley
President and CEO

[4] http://www.americanchemistry.com/s_acc/sec_article_acc.asp?CID=2178&DID=9939

Attachment A

Discussion of Additional Scientific Topics
Relevant to Endocrine Disruption Issue

Regulation of Endocrine Disruptors Must Be Based on Adverse Effects: It is important to recognize that the concept of "endocrine disruption" encompasses both an endocrine mechanism of action and adverse health effects. Finding that a chemical may interact with a component of the endocrine system does not necessarily mean that an adverse effect will ensue. Given the right dose and timing of exposure, almost anything – including everyday food – can, and often does, elicit an endocrine system mediated response that can be observed at a mechanistic or biochemical level. It is important to understand that natural variations in hormone levels and reversible or transient changes that are not considered adverse have been well documented. The concept of "endocrine disruption" applies only when two criteria are met: demonstration that 1) the primary biological mechanism of action is via an endocrine system pathway and 2) adverse health effect(s) are directly caused by a substance's interaction with that pathway. Mechanistic information alone is insufficient to evaluate the potential health significance of exposure to chemicals. Certain interactions or responses will be within the range of normal homeostatic response, and these are not adverse effects.

This is why, under the EPA's Endocrine Disruptor Screening Program (EDSP), Tier 1 screening (which will identify the potential for a substance to interact with the endocrine system, i.e. a mechanistic response) cannot be the basis of regulation. The EDSP Tier 2 testing, which determines the potential for adverse effects, and delineates the dose response for such effects, provides the needed data for hazard evaluation. This is a well recognized principle clearly articulated by the EPA's Endocrine Disruptor Screening and Testing Advisory Committee and subsequently codified by EPA in the Agency's EDSP. When hazard data are coupled with exposure data, the ensuing risk assessment provides the quantitative benchmark needed to evaluate the potential health significance of exposures, including exposures via drinking water pathways. This approach is consistent with the well-established scientifically sound procedures for assessing and managing risks that EPA employs under the SDWA to set national health-based standards for drinking water. Regulation should continue to be based on adverse effects, dose response and risk assessment.

Effects Mediated by Endocrine Disruption Pathways Are Covered in Outcomes from Toxicity Tests: It is also important to point out that even if specific endocrine screening has not yet been conducted on certain compounds, hazard identification based on observable outcomes from apical toxicity tests (i.e., outcomes such as pathologic states indicative of disease conditions) covers all modes of action, including endocrine pathways. As noted above, endocrine

disruption is not a distinct toxicological hazard per se, but a mode of action (MoA) of toxicity that could potentially result in a hazard, typically manifesting in the reproductive system.[5]

ACC members are committed to develop, produce and put into the marketplace products that are both beneficial and safe for humans and the environment. Accordingly, science-based evaluations of chemicals are necessary both to determine efficacy and safety for intended uses. In this regard, the toxicity information developed by ACC members as part of the High Production Volume Challenge Program, as well as other programs, is directly relevant to evaluating risks to children's health, including potential effects mediated by endocrine pathways, because it includes: 1) identification and definition of possible hazards upon all major organ systems from both acute and repeated exposures; 2) detection of potential hazards arising from *in utero* exposures; 3) evaluation of potential of a substance to affect reproduction; and 4) evaluation of the potential of a substance to damage DNA. Acute toxicity studies are most critical to assure correct packaging, labeling and handling to prevent poisoning incidents. Developmental and reproductive toxicity studies are most relevant for assessing risks that could affect normal prenatal and postnatal growth, development and maturation. It is these endpoints that are of most concern for endocrine disruption.

For evaluating the potential of a substance to cause adverse effects via endocrine-mediated pathways, a weight of evidence approach is considered to be the best scientific means to assess and integrate the range of available toxicity information. This approach considers not just the EDSP Tier 1 screening assays, but also the results of all other existing, relevant and validated toxicity tests such as subchronic, reproductive toxicity, and developmental studies. With this scientific analysis, in particular the laboratory toxicity studies investigating dose response of adverse health effects, there is assurance that the most relevant and best available science is used as a basis for regulatory decision making and setting health-based environmental standards. In such a weight of evidence evaluation, objective criteria are first employed to determine data quality and study reliability, and then a systematic evaluative process is applied for assessing the overall weight of the evidence for the postulated mode of action and dose response of adverse effects. In this way all relevant toxicity data can be comprehensively reviewed, given appropriate weight, and integrated in a manner that provides a robust, biologically plausible understanding of the potential hazards and health risks that exposures to a substance could pose.

Status of Scientific Debate on the "Low Dose Hypothesis": In the late 1990s, some scientists asserted that environmental exposure to compounds that could mimic hormones were capable of causing effects in lab animals at "low doses" and that these effects had not been detected earlier because the standard toxicology studies had been performed at high doses. This is the so called "low-dose" hypothesis – that low doses produce certain effects that are not seen at high doses.

There has been a considerable number of comprehensive, expert panel, reviews of this hypothesis over the last 10 years. In his comprehensive review of the scientific literature, Dr.

[5] ECETOC report TR106 "Guidance on Identifying Endocrine Disrupting Effects Technical Report No. 106, Brussels, June 2009.

Michael Kamrin, emeritus professor of Michigan State University, reached a clear finding that, "Based on the evidence, it is concluded that these "low dose" effects have yet to be established, that the studies purported to support these cannot be validly extrapolated to humans, and the doses at which the studies have been performed are significantly higher than the levels to which humans are exposed" (*International Journal of Toxicology*, 26:13–23, 2007).

The U.S. EPA in 2002 also carefully considered the entire body of scientific information available on the "low dose" hypothesis and concluded, "Until there is an improved scientific understanding of the low-dose hypothesis, EPA believes that it would be premature to require routine testing of substances for low-dose effects in the Endocrine Disruptor Screening Program. See: http://www.epa.gov/endo/pubs/edmvs/lowdosepolicy.pdf.

The media coverage of the scientific debate around the "low dose" hypothesis has been confusing and has tended to continue to "stir the pot" on this question. Therefore, it's important to clarify that at the present time, a considerable body of credible scientific evidence leans against the "low dose" hypothesis and therefore against changing the way chemicals should be tested in the endocrine program. This is the scientific process at work. The call to stay true to the scientific method and follow the data rather than "strong convictions" was most recently demonstrated in a statement from one of the leading researchers on endocrine disruptors, Dr. Richard Sharpe, on the recent studies published by EPA's lab showing no such "low dose" effects. See: http://toxsci.oxfordjournals.org/cgi/content/full/114/1/1

EPA's endocrine research lab recently published results of their studies focusing on very early stages of life in rodents and that found no such "low dose" effects on the brain, reproduction or development, and concluded that this lack of effects confirms "other robust, well-designed, properly analyzed multigenerational studies" ((Toxicological Sciences 114(1), 133–148 (2010)). This research by EPA scientists has been described in the leading scientific toxicology journal as "unequivocal and robust and are based on a valid and rational scientific foundation" See: http://toxsci.oxfordjournals.org/cgi/content/full/114/1/1

Based on the totality of this information, ACC believes that the overall weight of the scientific evidence clearly indicates there is no need to change the toxicity testing dose-setting approach or risk assessment methods because: 1) the low-dose findings have not been demonstrated consistently across different studies of the same substance in independent laboratories; 2) the findings are not consistent for all substances with similar mechanisms of action; and, 3) the biological significance of the reported low-dose effects is scientifically uncertain, in particular with respect to relevance of such effects, if any, to adverse effects upon health of the organism.