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Dear Dr. Schwartz,

We are writing to express significant concerns with the National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) management and review process for evaluating the reproductive and developmental effects of chemicals. It has recently come to our attention that CERHR is managed by a private consulting firm, Sciences International (SI), a company with historic ties to the tobacco industry and a client base that appears to include manufacturers of substances that might be subject to CERHR review, including the chemical up for review on March 5, 2007, bisphenol A (BPA). We think that the public would be very surprised to learn that industry consultants are managing critical public health agencies.

The ties between SI and industry raise important ethical issues that we describe in detail below. The fundamental question raised by the BPA case is whether or not government health assessments should be managed by private consulting firms with ties to the industry that manufactures the chemicals under review. We are very concerned that this relationship may influence the outcome of the BPA assessment.

These concerns are heightened by the Conflict of Interest policy document we received from Michael Shelby, the director of CERHR. In contrast to the CERHR policy for panel members who must disclose all potential conflicts of interest, the CERHR policy for consultants, sent to us by Mr. Shelby, states plainly that, "No specific restrictions are placed on the contractor." [1] This seems to mean that contractors with serious conflicts of interest would not have to disclose them and, in fact, could oversee analyses that could dramatically affect the future health and wellbeing of the American public. We would very much appreciate your clarification of this policy. Further, we request that prior to the March 5, 2007 meeting, SI and its employees disclose all potential conflicts of interest relative to BPA. Absent such disclosure, the integrity of the entire BPA review process will be in question.

In 1998, NTP established the Center for the Evaluation of Risks to Human Reproduction (CERHR) to "serve as an environmental health resource to the public and to regulatory and health agencies," and to provide "scientifically-based, uniform assessments of the potential for adverse effects on reproduction and development caused by agents to which humans may be exposed" via "rigorous evaluations of the scientific literature by independent panels of scientists." [2]

CERHR's mission is vital because five to ten percent of couples experience fertility problems, up to five percent of babies have birth defects, and a growing body of scientific evidence shows that exposures to industrial chemicals can impact reproduction and development. [3]

Environmental Working Group (EWG) was shocked to learn, therefore, that CERHR – a government agency under the auspices of the National Institutes of Health – is actually being run by a private consulting firm known as Sciences International (SI). To quote the SI website:

> "The most significant project at our firm is the management of the National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction, one of the premiere institutions for evaluation of reproductive and developmental health issues." [4]

This relationship is even more troubling because there are serious conflicts of interest and ethical concerns surrounding this contractor that involve apparent financial ties with the chemical industry and non-disclosure of these relationships.

On March 5, 2007 a CERHR expert panel is scheduled to evaluate the reproductive hazards presented by bisphenol A (BPA). This expert panel will be basing their decision on a 300-page document describing the hazards of BPA that was prepared by Sciences International. BPA is a heavily used industrial chemical that is integral to production of hard plastics and is found in the liners of metal food cans and in hard plastic containers. More than 200 animal studies show that BPA is toxic at very low doses. [5] The Centers for Disease Control has found BPA in 95 percent of people tested at levels that raise health concerns sufficient to warrant this major review by CERHR. [6] And the peer-reviewed science suggests that BPA may be contributing to increases in many adverse health conditions in the human population including breast cancer, prostate cancer and insulin resistance. [7-12]

Several ethical concerns surround SI's role in this process, including the company's financial ties to the chemical industry and their failure to disclose key information in the BPA review that may affect the expert panel's assessment of the chemical. These concerns are discussed further below.

SI conflicts of interest. SI appears to have a close working relationship with, and financial ties to, companies that manufacture the chemicals SI is charged with reviewing for CERHR. To our knowledge, SI has not disclosed these ties. As one example, in 2004, Anthony Scialli, the SI employee named as the lead SI manager of CERHR, co-authored a scientific paper with an employee of Dow Chemical Company on the critical issue of how animal test results can be applied to human health risk. [13]. Dow is a major producer of BPA. [14] The study was funded by the European Chemical Industry Council. There appears to be no way for the public to determine whether or not any SI clients are manufacturers or major users of BPA or any other chemical that may be reviewed by CERHR. SI notes on its website that its clientele comprise "approximately 50% public sector and 50% private sector clients." [15] Yet while SI lists the names of many of its public sector clients, SI's private sector clients are identified only as "various companies, trade organizations, and law firms." [16]

Scientists must sign conflict of interest forms before they may serve on a CERHR panel. [17] But CERHR's Director Michael Shelby indicates that "no specific restrictions are placed on the contractor."[1] This policy is in stark contrast to the disclosure procedures applied

to CERHR panel members, and is completely unacceptable. To earn the public trust, SI must disclose all financial and research ties that it has with any company or other entity that might have even a potential conflict of interest with the work carries out in its managing duty at the CERHR.

SI failure to investigate study funding sources. In its review document on BPA, SI fails to disclose industry funding sources and author affiliations for major studies cited in the document. For example, on page 177 in the document, SI states "[financial] support not indicated" for several important studies finding no adverse effects from BPA at low levels of exposure. [18] But, in fact, both studies are authored by scientists who routinely perform work for the chemical industry trade organizations: CEFIC-the European Chemical Industry Council and SPI-the Society of the Plastics Industry, both of which have member companies who manufacture or use BPA. [19] A simple request to these scientists would likely have revealed the source of funding.

SI's failure to identify the source of funding for these studies is more than just an oversight. A distinct pattern in BPA test results, relative to funding source, has been documented in the peer-reviewed literature, most notably in a 2005 review published in the National Institutes of Health journal *Environmental Health Perspectives*. This analysis examined more than 100 peer-reviewed studies on BPA and found a stunning relationship between funding source and study outcome: 100% of industry-sponsored studies found no adverse effects of BPA at low doses, compared to just 4% of independent studies. [20] Given the severe bias for industry-funded studies to find BPA "safe," funding sources for studies are a key piece of information the CERHR expert panel should review in making determinations on study utility. Without this information, CERHR assessments are incomplete.

The CERHR expert panel must have thorough information on study funding sources for the panel in order to make informed decisions on study utility. SI has failed to provide this.

SI failure to disclose key study limitations. In its review of BPA studies, SI scientists fail to document known, glaring design deficiencies that make it nearly impossible for certain studies to detect BPA toxicity. Without this information, in some cases the expert panel has issued glowing endorsements of seriously flawed studies, including a study [21] deemed by the expert panel to be "exceptional" and "very useful," when in fact the researchers in this study used resistant animals and animal feed that is known to mask the toxicity of chemicals like BPA. To quote the SI document: "This exceptional study is very useful for the evaluation process, and will carry significant weight in the evaluation of structural, histogenic, and fertility endpoints." [22]

In another example, the expert panel found a study "very useful in the evaluation" when, in fact, the National Toxicology Program (NTP) had noted issues with the study design that cast the findings into doubt, including the quality of the feed, concerns with animal weight, and data strongly suggesting that the particular experimental animals used would be insensitive to BPA's effects. [20, 23, 24] SI did not note these concerns in its review.

The CERHR expert panel is asked to review the usefulness and quality of literally hundreds of studies summarized in the SI review. The panel members cannot feasibly review each study individually, and therefore must rely heavily on SI interpretations. Therefore, it is critical for SI to thoroughly and accurate document study findings and deficiencies. Their

failure to do so in the case of these key studies can inject critical bias into the review process and severely inhibit the expert panel's ability to make sound decisions.

SI's history as industry consultant. SI's history of compromised ethics leads to deep concerns about its role in managing CERHR chemical assessments. In September, 2006 the journal *Environmental Science & Technology* (*ES&T*) detailed SI's dealings with the tobacco giant RJ Reynolds and its efforts to prevent the Environmental Protection Agency (EPA) from tightening its regulation of a toxic pesticide. [25] *ES&T* wrote that:

> In December 1998, the U.S. EPA proposed several risk-mitigation measures to protect workers handling phosphine—a chemical for fumigating grain and other commodities. The proposals included creating a buffer zone around fumigation sites and notifying residents living within 750 feet. EPA also proposed lowering the exposure threshold of phosphine from 0.3 parts per million (ppm) to 0.03 ppm. Court documents show that, to fend off regulations, RJ Reynolds Tobacco Co. (RJRT) funded the Phosphine Coalition, which successfully fought against the proposed changes. A centerpiece of its strategy was hiring the consulting firm Sciences International to lobby EPA and to write a study on phosphine's toxicity.
>
> The study was finally published in Risk Analysis in 2004. Five people appear as authors on the paper: Betty Anderson and two of her employees at Sciences International, and Joel Seckar and Paul R. Harp, who are listed as members of the Phosphine Coalition of Washington, D.C. The Phospine Coalition does not have a street address, and the paper does not note that Harp and Seckar are employed by RJRT.
>
> In April 1999, officials with Sciences International met with EPA staff to try to persuade the agency to halt the proposed changes to phosphine regulations. A month later, Anderson, Sciences International's executive director, sent a memo to Seckar stating, "I believe that the approach with the greatest likelihood of affecting EPA's position is to prepare and publish in a peer-reviewed journal a scientific paper or article that describes the current science on the toxicity of phosphine." She continues, "Since I am currently Editor-in-Chief of the international journal Risk Analysis, perhaps the peer-review process could be expedited, if we decide that it is the journal of choice."
>
> At the end of 1999, RJ Reynolds released a report highlighting the company's accomplishments. "R&D led the Phosphine Coalition in addressing the scientific issues involved when the Environmental Protection Agency (EPA) proposed a new phosphine exposure standard," reads a passage. Further along, the document states, "The efforts of the Coalition saved RJRT many millions of dollars."

Clearly, serious questions are raised when a company with this history is charged with running a government program vital to the protecting public health.

SI involved in all aspects of running CERHR

It is clear that SI is deeply involved in all aspects of CERHR, from selecting expert panel

members, setting the agenda for panel meetings, preparing the literature reviews, and helping to draft the panel's reports. The intimate and unusual relationship between the firm and CERHR is extensively documented. For example:

- CERHR's website describes the agency's structure as follows: "Under the direction of Michael Shelby, Ph.D., Director, CERHR at NIEHS, scientific and support staff at NIEHS and Sciences International, Inc. operate the Center for the Evaluation of Risks to Human Reproduction (CERHR). The Principal Investigator, Anthony Scialli, M.D., leads the scientific and support staff at Sciences International, Inc." [26]

- The website of Sciences International states that: "The most significant project at our firm is the management of the National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction, one of the premiere institutions for evaluation of reproductive and developmental health issues." [27]

- Although Dr. Scialli is the Vice President of SI, on CERHR's on-line "contact" page his affiliation is listed simply as "NTP Center for the Evaluation of Risks to Human Reproduction." [28]

- The Federal Register notice describing the creation of CERHR explains that: "Scientists representing NTP agencies and Sciences International, Inc., the contractor who will support the Center, will constitute a core committee which will provide the initial review for [panel member] nominations, select the expert panel membership and establish the meeting agenda." [29]

- Expert panel and chemical nominations are sent directly to the SI offices. Some CERHR workshop sessions take place there as well. [30, 31]

For its work –and influence –SI gets paid heftily. The firm's current contract, which runs from June 2003 through June 2008, is worth $5,241,109. [32]

It is not uncommon for federal agencies to contract out certain pieces of work to consulting firms or other contractors. However, we are unaware of any other instance in which nearly all of the functions of a pubic health agency have been outsourced to a private entity. Please provide us with details on when this has been done previously and what the bidding parameters were.

It is also unclear whether the SI contract was put out to bid. If it was put out for competitive bid, please provide us with the bid notice and parameters. If it was a no bid contract, please explain the rationale for this decision.

The arrangement between CERHR and SI raises serious ethical questions that demand immediate disclosure of financial and research ties to chemical manufacturers and other industries that make or use substances under review by the CERHR. These disclosures must apply both to individual SI staff as well as the greater institution. Questions about the objectivity and adequacy of this review process and the reviewers must be resolved before a final decision on BPA is reached.

It is also critical that CERHR incorporate into its final decision on BPA critical input from an NIEHS-sponsored expert workshop convened in November 2006. Forty-two leading scientists on the effects of BPA at low doses reviewed existing literature on the issue (see

attached list). The experts are producing a series of papers addressing the very issues being reviewed by CERHR, but expect to have only two of them completed by the March 5th meeting. It is our understanding that these experts are seeing a pattern of adverse effects at low levels of exposure similar to those measured in humans by the Centers for Disease Control and Prevention [33]. We are concerned that CERHR is poised to make a decision on BPA prior to the review of this important information.

Regulators, policy makers, and the general public desperately need the "readily accessible, scientifically authoritative" evaluations of potential reproductive and developmental toxins that CERHR is supposed to be providing. [34] But these evaluations will only serve to help protect human an environmental health if they are truly objective and trustworthy. Given that bisphenol A is found in consumer products as diverse as baby bottles, food-can linings and dental sealants, this is a question that the public has a right –and a need –to know.

Sincerely,

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Executive Director
Environmental Working Group

Cc: Mike Leavitt, Secretary, U.S. Department of Health and Human Services
John Howard, M.D., M.P.H., J.D., LL.M., Director, National Institutes of Occupational Safety and Health, Centers for Disease Control, U.S. Department of Health and Human Services
Andrew C. von Eschenbach, M.D., Commissioner, U.S. Food and Drug Administration
William Slikker, Jr., Ph.D., Director, National Center for Toxicological Research, U.S. Food and Drug Administration
Michael Shelby, Ph.D., Center for the Evaluation of Risks to Human Reproduction, National Toxicology Program
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Representative Tom Davis, Ranking, Committee on Oversight and Government Reform
Representative John Dingell, Chair, Committee on Energy and Commerce
Representative Joe Barton, Ranking, Committee on Energy and Commerce
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