

**Testimony of  
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**before the  
House Subcommittee on Energy and Environment**

**“Endocrine Disrupting Chemicals in Drinking Water:  
Risks to Human Health and the Environment”**

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**Background and Expertise**

I sincerely thank the Subcommittee for inviting me to testify. I am pleased to be given the opportunity to address you regarding endocrine disrupting chemicals and their potential human and environmental health risks.

It has been almost 20 years since I first began tracking the scientific literature on the endocrine effects of environmental chemicals, and since then, I've devoted a significant portion of my professional career as a pharmacologist and toxicologist to this issue.

My work generally involves evaluating the relationship between basic research discoveries and their application to real world problems, especially health risks posed by chemical substances.

My expertise is typically sought by private individuals and firms who rely on an accurate understanding of the relationships between basic research and health risks to ensure the safety of products they bring to the marketplace. These are primarily manufacturers of industrial chemicals, pesticides, pharmaceuticals, cosmetics, dietary supplements, and other chemical substances, and their trade associations and legal counsel.

Today, I am here of my own volition and represent only myself. My testimony is based on my my scientific training and expertise and my own experience with the issues at hand.

I have given special attention to the subject of evaluating potential health risks posed by combined exposures to multiple chemicals, such as may occur from drinking water. As someone knowledgeable in these areas, I have been invited to advise governmental agencies and organizations on such issues.

In December of 2008, I addressed a workshop of the National Research Council investigating the issue of evaluating exposures and risks posed by mixtures of pharmaceuticals in the water supply.

I've been a part of several working groups convened by professional and scientific societies interested in endocrine issues. From 1996 - 1998, I served on the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), which was the Federal Advisory Committee to EPA that initially devised and recommended the two-tiered endocrine screening and testing program that it has now begun to implement.

I served on the EDSTAC as the representative for small business stakeholders, and I also served on the workgroup of that committee charged with evaluating and recommending the specific screening assays that comprise the Tier 1 Screening Battery.

In keeping with the Congressional mandate for EPA to use validated test systems in constructing its screening program for estrogen-like effects in humans, the EDSTAC recommended to EPA that it undertake a formal validation program for the proposed screening and testing batteries. EPA did so, using the EDSTAC final report as its template.

Since my EDSTAC experience, I have followed closely the EPA and OECD validation programs for the endocrine screening assays comprising the Tier 1 screening battery, now ordered to be conducted on an initial set of 67 chemicals.

I have assisted various industries in following this validation program, and I also served on an OECD peer-review panel that evaluated the validation program for the uterotrophic assay, one of the mainstays of the endocrine screening battery.

Just to make sure, you will remember that the Tier 1 battery of assays is intended to be a preliminary screen used to select items that could then be tested in the more specific Tier 2 battery of tests.

It is about this Tier 1 endocrine screening battery that I wish to focus my comments to this subcommittee. In doing so, my first objective is the most necessary clarification of some common misconceptions about the Tier 1 screening battery and the validation program conducted for the Tier 1 screening assays.

### **Basic Scientific Principles are Applicable to Endocrine Screening**

Dispelling misconceptions is essential in order to see clearly what this endocrine screening program offers, and what it does not offer, and thus, to consider how the program might best be utilized.

In order to do that, I will review some of the most basic tenets that validate scientific information so that the existing knowledge base on the endocrine screening battery, and on endocrine disruption in general, can be understood in its proper context.

For data to be considered an established scientific observation, it must, at a minimum, conform to three fundamental tenets that have been well explained by Dr. Gio Gori, formerly Deputy Director of the Division of Cancer Cause and Prevention at the National Cancer Institute. These three tenets are simple, understandable, and undeniable, applying to the basic language of science that enables reliable measurement of the natural world.

**First**, the identity and authenticity of scientific measurements must be verifiable within a defined range of precision. In other words, we must be able to demonstrate unequivocally that we have measured what we claim to have measured and that we know the margin of error on our measurements.

**Second**, measurements and observations must not be confounded by extraneous factors and influences known to corrupt their accuracy and precision. In other words, we must be able to demonstrate that our measurements are taken under well-controlled conditions.

**Third**, the measurements and observations must be replicable in independent hands. In other words, other scientists using the same or similar methods must be able to repeat the results.

These three tenets are common sense, but often become confused amidst the technical complexity and nuanced jargon of modern science, even by scientists.

It is in the context of these simple, common-sense tenets that the opportunities and pitfalls of the endocrine screening program must be understood. This is also the context in which I explained to the National Research Council what valid methods exist for evaluating cumulative risks of pharmaceuticals in the water supply.

### **Correcting Misperceptions Concerning Validation and Implementation of the EDSP Assays and the Tier 1 Battery**

**First, regarding validation of the endocrine screening assays, validation and subsequent implementation of the EDSP has not been unreasonably delayed.**

While there is no disputing that validation programs for these assays have been protracted and have required more in-depth experimentation than initially envisioned by some individuals who served on EDSTAC, this lengthy process was completely predictable given the complex biology of the systems these assays were intended to measure.

The Tier 1 endocrine screening battery includes 11 separate assays that range from single-day procedures conducted in the laboratory to multi-week assays requiring many experimental animals, large animal housing facilities, many personnel to care for and observe the animals, animal surgeons, and the evaluation of numerous tissues and organs by fastidious histopathological methods.

Scientists who understand the process of scientific validation - i.e., that the results of the assay conform to the three tenets described above and are relevant to their intended purpose - expected a much longer validation process due to the ambitious nature of the proposed endocrine screening program and the need to answer a number of important questions regarding the sensitivity and specificity of the individual assays and the battery as a whole, since the battery was intended to be interpreted as a unit.

Unfortunately, because of time-constraints imposed on EPA by Congress, the Agency conducted the minimum validation work that might satisfy the Congressional mandate to use validated test systems so that screening could begin.

The complexity of many of these assays and the novel uses to which they are being put in the Endocrine Screening Program - the detection of potentially weak hormonal activity for a broad array of diverse chemical types and molecular structures - fully accounts for the decade needed to complete even the abbreviated validation program that was conducted on these assays.

It must be appreciated that neither EPA nor any scientist or scientific body is able to dictate the results of scientific research and the timeframe on which it will yield useable results. To my knowledge and from my perspective, EPA worked as rapidly as it could, taking advantage of cooperative efforts by the OECD and other international organizations, to conduct validation experiments and to adjust the experimental plan as necessary based on results of the studies as they were obtained. Some results enabled rapid progress; other results dictated abandoning initial approaches and evaluating alternatives instead. Scientific results simply cannot be force-fit to meet a predetermined schedule.

**Second, and perhaps more unfortunately, the endocrine screening battery, as a whole, has not yet been shown to be useful for its intended purpose.** Because many of the assays are protracted and complex, the expedited validation programs were able to focus only on the ability of the individual assays to detect known positive and negative endocrine active compounds specific to each test. Only limited testing of unknowns was possible given the

intense pressure on the Agency to implement the screening program rapidly. Moreover, the performance of the battery as a whole has been left unaddressed.

Validation efforts for some of the assays, the pubertal male and female assays in particular, were unable to verify that the assays could yield negative results for a range of chemicals lacking endocrine activity. Indeed, the criteria for interpreting ambiguous results had to be modified in order to claim that these assays could yield a negative result for even one chemical.

The assay protocols left standing at the end of the validation exercises, which have now been formalized as EPA test guideline series 890, leave unaddressed a number of technical problems that will complicate and confound the development of interpretive criteria for the individual assays as well as for the battery as a whole.

In short, the validation process has provided increased confidence that we are measuring what we claim to measure with the endocrine screening assays, but the precision of some of those measurements is still uncertain, and the conditions under which extraneous factors might influence the measurements are not well controlled in all the assays. This makes tenuous the assumption that the screening battery will actually differentiate chemicals with the potential to interact with the endocrine system in definitive studies from those that do not.

Presently, no one knows how useful the endocrine screening battery will be, as a whole, for predicting which chemicals should undergo definitive testing and which should be considered a low priority for further analysis of endocrine effects. If the endocrine screening battery forwards everything to further testing, it has absolutely no utility whatsoever.

EPA, on the advice of its Scientific Advisory Panel, has attempted to address this problem by ordering an initial phase of EDSP screening on 67 pesticide chemicals. The purpose of this approach is to evaluate the Tier 1 assays and battery, as well as the Agency's policies and procedures, using a discrete set of chemicals. To be an effective approach, additional screening must await completion of the initial phase, at which time EPA would modify its assays, battery and procedures as necessary.

Make no mistake; the status of the endocrine screening battery is analogous to a new but unproven clinical screening procedure. Assuming that a precautionary approach is without harm and that all important decisions will await the definitive test ignores the very real fact that life altering decisions are made daily on the basis of clinical screens. There are consequences to getting it wrong, even if it is only a screen and not the definitive test.

In the same way, we might inadvertently presume great risk for relatively safe chemicals, and instead use riskier replacements, simply because some chemicals were assumed to be harmful based on highly publicized endocrine screening results. As a scientist who is also a father, a consumer and operator of a small business, I would like to know that products in commerce are evaluated on the basis of real risks, demonstrable by objective science, not upon hypothetical connections between screening results and serious diseases that are easily and conveniently sensationalized.

**Third, endocrine screening will not identify “endocrine disruptors.”** This issue concerns the predictive value of the endocrine screening battery and whether so called environmental endocrine disruptors have been unequivocally identified. Highly publicized statements have been made repeatedly over the years declaring that serious human diseases are known consequences of exposure to environmental endocrine disrupting chemicals. These speculations have often been made on the basis of epidemiological studies that used methodologies appropriate for hypothesis generation but wholly incapable of confirming putative associations or demonstrating causes. Interestingly, the list of human disease associated with

endocrine disruption has shifted as initial speculations were debunked or severely tempered - breast cancer related to chlorinated organic chemicals; reduced sperm counts related to higher chemical exposures in industrialized nations; feminized male fish in UK rivers caused by exposure to soaps and detergents - only to be replaced by newer and relatively less scrutinized speculations. Rather than convincing us by the sheer number of speculations that are based on hypothetical studies, the failure to reproducibly demonstrate these associations and to support a true causal role for chemical exposures should lead us to suspect them.

There is also a widely held misconception that the endocrine screening battery provides a sensitive means of identifying chemicals that may cause subtle health effects in the human population or in wildlife. Since those subtle effects have not been demonstrated, nothing could be more misrepresentative of what the screening battery can be expected to do. Indeed, the endocrine screening battery is intended to detect only chemicals that have the potential to interact with the endocrine system in live animals; it does not and cannot test for adverse health effects.

Interaction with the endocrine system *per se*, i.e., positive results in the endocrine screening battery, does not signify that adverse endocrine effects are likely. The endocrine system is a homeostatic system that functions to maintain relatively consistent internal body conditions. An endocrine response is merely an indication that the system is working. The endocrine screening battery utilizes this responsiveness to screen chemicals for potential interaction with the system, but it does not determine whether the endocrine system is merely responding or is irrevocably perturbed by the chemical. The endocrine system is like a thermostat on a heating and air conditioning system; the fact that it turns off and on many times during the day does not signify that it is damaged, but merely that it is responding to changes in room temperature. Without knowing whether room temperature was properly controlled, it is impossible to conclude that the thermostat or heating system malfunctioned.

In the same way, the endocrine screening battery cannot determine that a chemical poses a risk to human or environmental health, but merely indicates that some component of the endocrine system recognizes the presence of the chemical. A more thorough analysis - tier 2 tests - must be conducted to determine whether that potential interaction with the endocrine system leads to adverse effects. It may for some chemicals, but for many it might not, or if so, only at doses that far exceed doses that produce some other serious toxic health effect. In the latter case, adverse endocrine effects would never be observed.

This last case underscores another reason the endocrine screening battery cannot be interpreted as indicating adverse effects: the extraordinarily and unrealistically high doses of chemicals that will be used in screening may elicit responses that could never occur at lower levels typically encountered in the environment. A similar conclusion, and others, have been explained in a recent publication by Dr. Richard Sharpe of the UK, who was one of the original voices of concern for the possible effects of environmental endocrine disrupting chemicals.

These basic pharmacological and toxicological concepts of dose-response were at the core of my presentation to the National Research Council concerning risks posed by mixtures of pharmaceuticals in the water supply. These concepts have not been supplanted by hypothetical low-dose theories or by the speculation that mixture effects observable at high doses also operate and manifest adverse effects at low, environmentally relevant levels of exposure.

Although good health trumps money in my value system, it is nevertheless important to recognize that endocrine screening is very expensive and should not be required of more than the initial 67 chemicals until its utility has been demonstrated. The costs of screening alone are on the order of 1 to 1.5 million dollars per chemical, but this figure does not account for the full cost to consumers who ultimately must bear the burden of funding the activities of the EPA and

Congress on this issue, nor does it include the costs of conducting tier 2 testing on chemicals that are false positives in the screens. Finally, such monetary figures fail to give due consideration to the tens of thousands of laboratory animals that must be sacrificed to conduct this screening, and the tens of thousands more that will be sacrificed in tier 2 testing.

Four months ago, in October of 2009, EPA began issuing Tier 1 test orders for 67 chemicals comprising pesticide active ingredients and inert ingredients in pesticide products. Many of these chemicals have already undergone the more extensive, long-term animal tests typical of tier 2 that are capable of defining adverse effects on reproduction and development in rodent species. Thus, it can only be hoped that the initial round of test orders will yield data upon which the predictive utility of the endocrine screening battery for adverse effects in laboratory rodents may finally be evaluated.

Expanding the program within the first year of its implementation, as has been proposed, will not only be costly, but it will needlessly squander an opportunity to evaluate the data from the first 67 chemicals screened and to improve the screening battery based on those results. In short, premature expansion carries great risk of getting the science wrong, with the consequence of poor decision-making that imperils rather than protects public health and the environment.

From a scientific perspective, precious resources would be better directed toward evaluating the utility of the endocrine screening battery for identifying adverse endocrine effects in laboratory rodent tests, which are known to capture adverse effects on reproduction and development mediated by all physiologically relevant pathways, including endocrine disruption.

Rather than expanding the program prematurely, this path would allow EPA time to determine the best criteria for moving chemicals from tier 1 screening to tier 2 testing based on the data, and to determine whether enhancements, deletions, or replacements for the current assays are needed.

Without such a deliberate approach that relies on established scientific principles rather than on precautionary rhetoric and speculative hypotheses, the credibility of the endocrine screening program and the government agencies that drive it is likely to suffer.