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I am submitting a formal comment to ICCVAM/NICEATM about a problem that has existed for at least a year with respect to the NIH evaluation of SBIR proposals involving the use of cell based assays to detect chemicals that interact with the estrogen receptor (ER) and/or androgen receptor (AR) (i.e., proposals that are hazard assessments). If scored sufficiently low in the NIH "golf-score model", hazard assessment SBIR grants are evaluated by a single Scientific Review Group (**SRG**) panel (currently ZRG1 EMNR-W(10), if they are Phase 1, Phase 2, or Fast-Track applications, and are typically funded by NIEHS. ***In brief, contrary to NIEHS, NTP, and ICCVAM/NICEATM goals to improve and automate in vitro testing[2-6], hazard assessment proposals are unfavorably reviewed by some panel members because they do not include an assessment of risk to humans[1].*** Other panels recently convened to evaluate Phase 2B applications [ZRG1 ETTN-C (56), ZES1 LWJ-D (U4)] have exhibited the same problem with requiring risk-analysis assessments for purely hazard assessment proposals.

I believe the following hazard versus risk analysis points are relevant for the NIH Center for Scientific Review (CSR)--- as well as for NIEHS, and NICEATM/ICCVAM:

1. The purpose of a hazard assessment is to characterize whether or not, and to what extent, a chemical or physical agent has the ability to cause a biological effect of interest; for example, detecting chemicals that up- or down-regulate the ER using appropriate cell models. A risk assessment would use that data as well as other data (e.g., exposure, environmental persistence) to predict the level of risk to the human population or to the environment. For example, the U.S. National Toxicology Program at NIEHS conducts hazard assessments while the U.S. EPA conducts both hazard and risk assessments, separately or combined. ICCVAM/NICEATM validation studies are hazard assessment studies.

2. ***Members of the single NIEHS SRG panel [and now other Phase 2B panels] consistently give very divergent scores to hazard assessment proposals that do not include risk analyses***. Please see **Attachments 1-3** that provide some relevant examples. Additional data can be provided, reflecting the same ideological commercial interest bias that should not exist in a scientific assessment.

3. The divergent scores are consistently driven in part by the insistence by some that hazard assessment in the absence of risk assessment has no value or is suspect or inadequate. This controversy is perhaps best described by two conflicting editorials published in different sets of scientific journals by Drs. Dietrich[1] and Gore[2,3] in which hazard assessments are characterized as "junk science" -- or not, respectively.

4. As given in detail in NIEHS mission statements[4,5] and detailed in a recent NIEHS video[6] featuring Dr. Birnbaum, NIEHS Director, NIEHS desires both hazard (primarily *in vitro*) or risk assessment (*in vivo*, including human) proposals for basic

science grants (e.g., R-01, R-21, etc.) and SBIR grants (e.g., R-43, R-44, etc,). Each of these research areas are recognized as having value as independent studies.

Part of the problem is that it appears in the case of the review of Phase1, Phase 2, or Fast-Track that there are no alternate panels, and a single panel reviews NIEHS grants in many areas so that expertise regarding hazard assessments are rather limited - - and hazard analysis assessments are **not** explicitly listed in the panel mission statement. Hence, expertise to review hazard assessment proposals often appears to be lacking (**Appendices 1A, 1B and 2**). A second problem is that validation of *in vitro* assays need follow a rather well proscribed set of protocols that by their very nature are not innovative--- and innovation is a major scoring factor for any NIH SBIR panel.

[1] Dietrich D.R. et al., *Scientifically unfounded precaution drives European Comission's recommendations on EDC regulation, while defying common sense, well established science, and risk assessment principals.* Arch. Toxol, 2013. 87: p. 1739-41.

[2] Gore A.C*., Editorial: An international riposte to naysayers of endocrine-disdrupting chemicals* .Endocinology, 2013. **154**: p.3955-56.

[3] Gore A.C. et al., *Policy decisions on endocrine disruptors should be based on science across disciplines: A response to Dietrich et al.* Endocrinology, 2013; **154**: p. 3957-60.

[4] NICEATM, *Funding opportunities and NICEATM desires for in vitro assays.* Available: http://ntp.niehs.nih.gov/pubhealth/evalatm/resources-for-test-method-developers/funding-opportunities/index.html. 2015. Accessed April 02, 2015.

[5] NIEHS, *National Institute of Environmental Health Sciences. Fact Sheet: Endocrine Disruptors.* http://www.niehs.nih.gov/health/materials/endocrine_disruptors_508.pdf. 2010. Accessed July 29, 2012.

[6] http://www.abc.net.au/catalyst/stories/4207313.htm