Learning By Doing – Phase I of the ToxCast Research Program. Robert Kavlock, National Center for Computational Toxicology, ORD/USEPA

In 2007, the USEPA embarked on a multi-year, multi-million dollar research program to develop and evaluate a new approach to prioritizing the toxicity testing of environmental chemicals. ToxCast was divided into three main phases of effort – a proof of concept, an expansion and confirmation, and finally, a reduction to practice. Phase I of the effort is now largely complete and results are being analyzed. This presentation will summarize a few key lessons learned along the way, all of them magnified by the scope of the assays being used and the numbers of chemicals being profiled. The first lesson was about data management.   Because the data were coming from a number of very diverse sources, and were of very diverse nature, a well designed and implemented work flow strategy and database system was required.   Accurate chemical information management and chemical structure annotation were deemed essential, involving the documentation of sample handling, and confirmation of the purity, salt form and stability of the chemicals. Standardized dictionaries, or ontologies, of terms were a critical need to ensure comparability of the animal bioassay data that was generated over the span of decades from multiple laboratories. The second lesson is that transparency is paramount. Data, both from the newer high throughput screening methods and the traditional assays against which they are being prepared, must be made available to the scientific community for independent analysis and interpretation. The ToxCast Data Analysis Summit of May 2009 was a major step in that direction, along with the posting of datasets on a public web site. Although the amount of data can be overwhelming, it is important to critically evaluate the individual results to detect nuances that could be missed with global analyses. A third lesson is that researchers need to take a careful look at unexpected results and attempt to refute or confirm those using alternate technologies in order to avoid unsupported conclusions and discern artifacts. Finally, it takes a true team effort to ensure that these various elements are appropriately addressed. Paying attention to lessons learned helps ensure that the research will progress on schedule, will deliver interpretable results, and will convince the broader scientific and stakeholder communities of the value of the findings. *This is an abstract of a proposed presentation and does not necessarily represent EPA policy.*