BOSC Review (Dec. 2007) of Computational Toxicology Research Program

Summary of Review Comments and ORD Response

Subcommittee

- Dr. George Daston (Chair)
- Dr. James Clark
- Dr. Richard DiGiulio
- Dr. Muiz Mumtaz
- Dr. John Quackenbush
- Dr. Cynthia Stokes

Goals of the Review

- To provide NCCT with advice on the progress the Center has made, in the past year, in fulfilling its mission and strategic goals.

- Particularly, the Subcommittee addressed six charge questions for five NCCT activities (ToxCast, Informatics Technology/Information Management (IT/IM) activities, Virtual Liver, Developmental Systems Biology, and Arsenic BBDR).

Summary of Charge Questions

- Does the scope and involvement of expertise in the project reflect activities consistent with the function of a Center?

- Are the goals and milestones suitably described, ambitious, and innovative?

- Are there significant gaps in the approach that can be pointed out at this point in the evolution of the project?

- Does the work offer to significantly improve environmental health impacts and is the path toward regulatory acceptance and utilization apparent?

- Have appropriate data management and analysis tools been incorporated into the project?

- How would you assess the outreach to other groups in executing the projects?

Overall Finding

"The Subcommittee was very pleased with the progress that the Center has made towards its goals. NCCT first became operational in February 2005; during the 2.5 years between its establishment and this review, NCCT has made substantial progress in establishing priorities and goals; making connections within and outside EPA to leverage the staff's considerable modeling expertise; expanding its capabilities in informatics; and making significant contribu-tions to research and decision-making throughout the Agency. We are pleased to see that informatics tools developed by the Center already are being used by program offices, and that the program offices are taking advantage of the expertise of the Center in developing critical elements for risk assessment…"

Summary of Specific Recommendations

- Stakeholder identification and involvement
- Discussions with risk assessment practitioners
- Develop effective ways of dealing with wealth of data
- Look for relevance of ToxCast^{TM} beyond toxicity prioritization including exposure paths and ecology
- Detailed milestones and time table
- Detailed project plans for v-tissues

Summary of Responses

- Stakeholders, risk assessment practitioners, and outreach
  - Identify and invite key stakeholders to next BOSC review
  - Regular discussions with NCEA and others are underway
  - Expansion of Communities of Practice
  - Project team for v-Liver project includes risk assessors
  - v-tissues workshop with European Union in April 2009 at EPA
  - ToxCast^{TM} data summit in May 2009 at EPA
    - Provide forum for external scientists to discuss with EPA alternatives for deriving predictive signatures from ToxCast^{TM}

Responses Continued

- Effective ways for dealing with data
  - Extensive suite of interactive databases is under development and prioritization of data input is in consultation with program offices and others
    - ACToR, (http://actor.epa.gov/actor) is the global repository of data that is relevant to environmental chemicals
    - ToxRefDB, *in vivo* toxicology data on chemicals in the ToxCast™ program
    - ToxMiner, a compilation of statistical tools capable of analyzing relationships between ToxCast™ and ToxRefDB data, and performing predictive signatures
    - the ToxCast™ chemical registry, used to track nominations for ToxCastTM screening, to track sample identity and sample QC, and fto link actual samples to ToxCast™ data
    - DSSTox, chemical structure layer added to the data sets

Responses Continued

- Relevance of ToxCast^{TM} beyond toxicity prioritization including exposure paths and ecology
  - Expanded workgroups to address exposure pathways through "ExpoCast" – exposure relevance to toxicity signature predictions
  - Partnering with NHEERL and NERL for HTS for ecological species other than human
  - Testing of pharmaceuticals in Phase II of ToxCast^{TM} to compare results to known human toxicities

Responses Continued

- Detailed milestones for projects and more detailed project plans for v-tissues
  - Milestones have been put in place for ToxCast^{TM,} v-tissues, and IT/IM and are included in an appendix to response memo
  - Short-term and long-term goals for v-Liver have been identified and are in response memo
  - Detailed project plan for v-embryo developed and in memo.
  - Milestones for BBDR for Arsenic have not been developed due to significant change in the plans for this work which has been described in memo
    - The lead and partner laboratory, NHEERL after considerable peer review and consultation with program office no longer are concentrating on this project
    - NCCT efforts being redirected to v-tissues and related projects

Next Steps

- NCCT is developing the next ORD Computational Toxicology Research Implementation Plan
  - Will cover 2009 – 2012
  - Will reflect recommendation from most recent BOSC review
  - Will be presented to BOSC Computational Sub-committee for review in 2009 (exact date TBD)
  - Milestones and plans developed as result of these recommendations will be incorporated