



## Computational Toxicology Research Program: Recent Program Accomplishments

- Completion of Phase I of ToxCast
- Release of ToxRedDB with five major data sets in relational format
- Release of ACToR website
- Launch of v-Liver and v-Embryo
- Increased dialogue with ORD Labs/Centers on tools of computational toxicology
- Establishment of interagency Tox21 consortium
- Hosted v-Tissues 2009 with the European Union under joint Biotechnology Agreement
- Chair of OECD Working Group on Molecular Screening
- Award (pending) of 4<sup>th</sup> STAR Computational Toxicology Center
- Highly consistent with Administrator's (and SPC) priority to improve contaminant assessment



# CTRP: Major Anticipated Accomplishments

- Publication of large series of papers on ToxCast Phase 1 assays and predictions
- First ToxCast Data Summit, May 14-15 in RTP
- Awarding additional ToxCast HTS contracts
- Co-Lead on EPA's Strategic Plan for the Future of Toxicity Testing
- Launch of Phase II of ToxCast
- Recruitment of Communications specialist
- Construction of 10,000 chemical screening library at NCGC under Tox21
- Expansion of data modules contained in ToxRefDB
  - Developmental neurotoxicity, potentially the EDSP Tier 1 Battery
- Publication of molecular docking models for identification of protein based targets (first ER, then AR and then moving to ToxCast protein targets)
- Release of Knowledgebases supporting v-Tissues
- Fourth review of the program by the BOSC – September 29-30, 2009

# CTRP: 2010 – 2014 Strategic Directions

- Second Generation CTRP Implementation Plan
  - Collapsing three long term goals to single on (Providing Computational Tools for High Throughput Exposure, Hazard and Risk Assessments)
  - Disinvestment of NRMRL related CTRP activities
  - Stronger cross MYP and L/C interactions Development and verification of predictive bioactivity profiles
  - Concentrated effort to launch of ToxCast Phase II (+700 chemicals)
  - Incorporation of failed pharmaceuticals and nanomaterials
- Initial efforts to develop exposure analogue of ToxCast (ExpoCast)
- Expansion of v-Tissue programs
- Continued support and growth of ToxRefDB and ACToR
- Discussion on future direction of the STAR Computational Toxicology Program as initial Centers expire
- Establishment of Contaminant IMD, based of Strategic Plan for Evaluating the Toxicity of Chemicals and spanning source to outcome to risk assessment
- The CTRP will continue to evolve as the research progresses. The greatest chance will be an extension of the high throughput hazard prioritization model pioneered by ToxCast to exposure and risk assessment. There will have to the concordant advances in approaches to targeted testing in order to best interpret and understand results from HTS.



## Computational Toxicology Research Program Significant Anticipated Products and their Intended Use by Partners

- ToxCast will be reduced to practice and provided to EPA program offices for use in prioritizing chemicals for toxicity testing; ancillary benefits will include information about common modes of action, susceptible genotypes and effects of mixtures
- ToxRefDB will become a living, central repository of animal bioassay data across the Agency, with accompanying ability to probe the relational database by endpoint, chemical class or syndrome.
- Two virtual tissues will be developed that will allow computer simulations of the effects of perturbations in molecular pathways on cellular and tissue function. These will be used in conjunction with pharmacokinetic models to exposure the shape of dose response relationship below the experimentally observable range.