



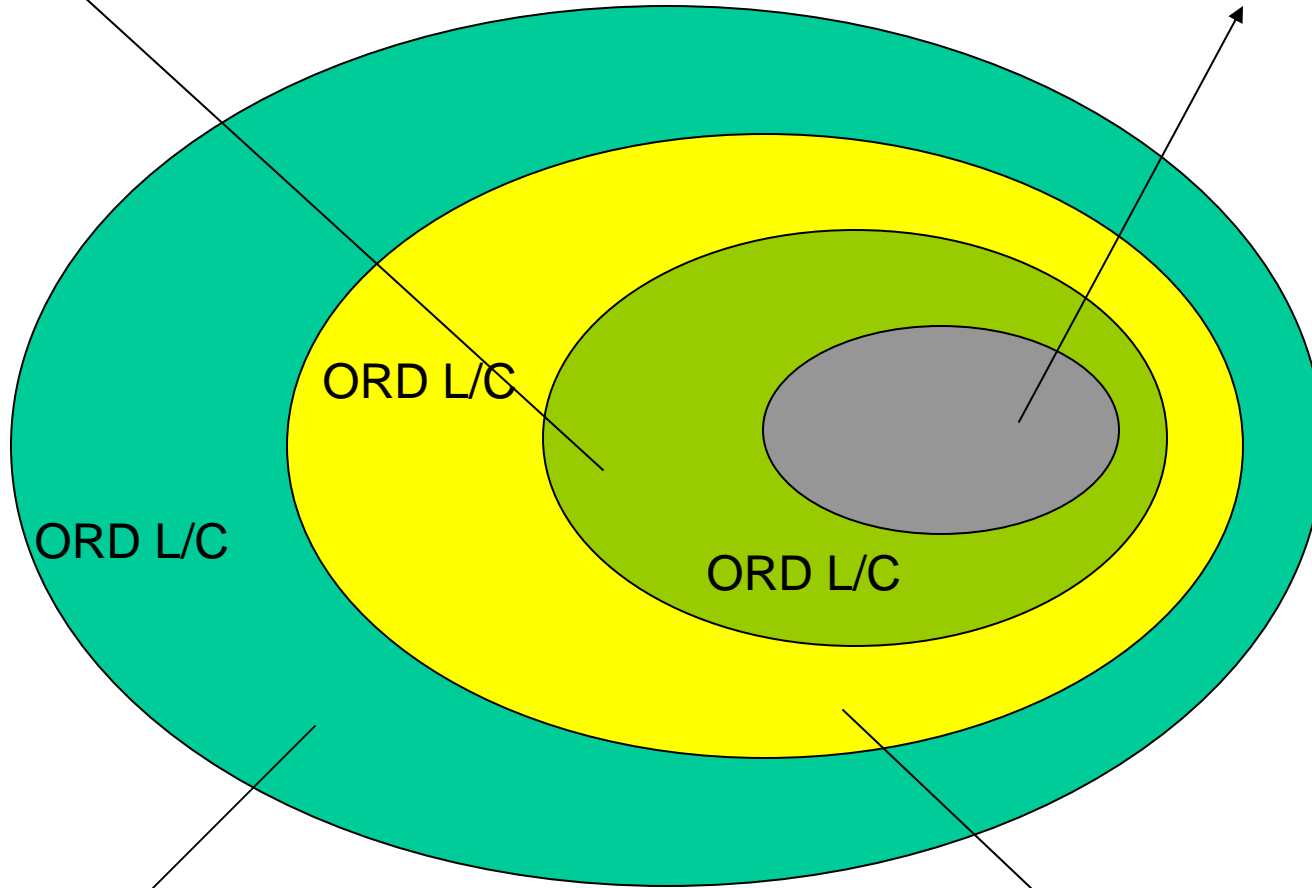
***Interactions by NCCT with ORD
Labs and Centers and Others***

**National Center for Computational
Toxicology**

Robert Kavlock and Jerry Blancato

CompTox Research Program

CompTox Center



ORD Research

April 25, 2005

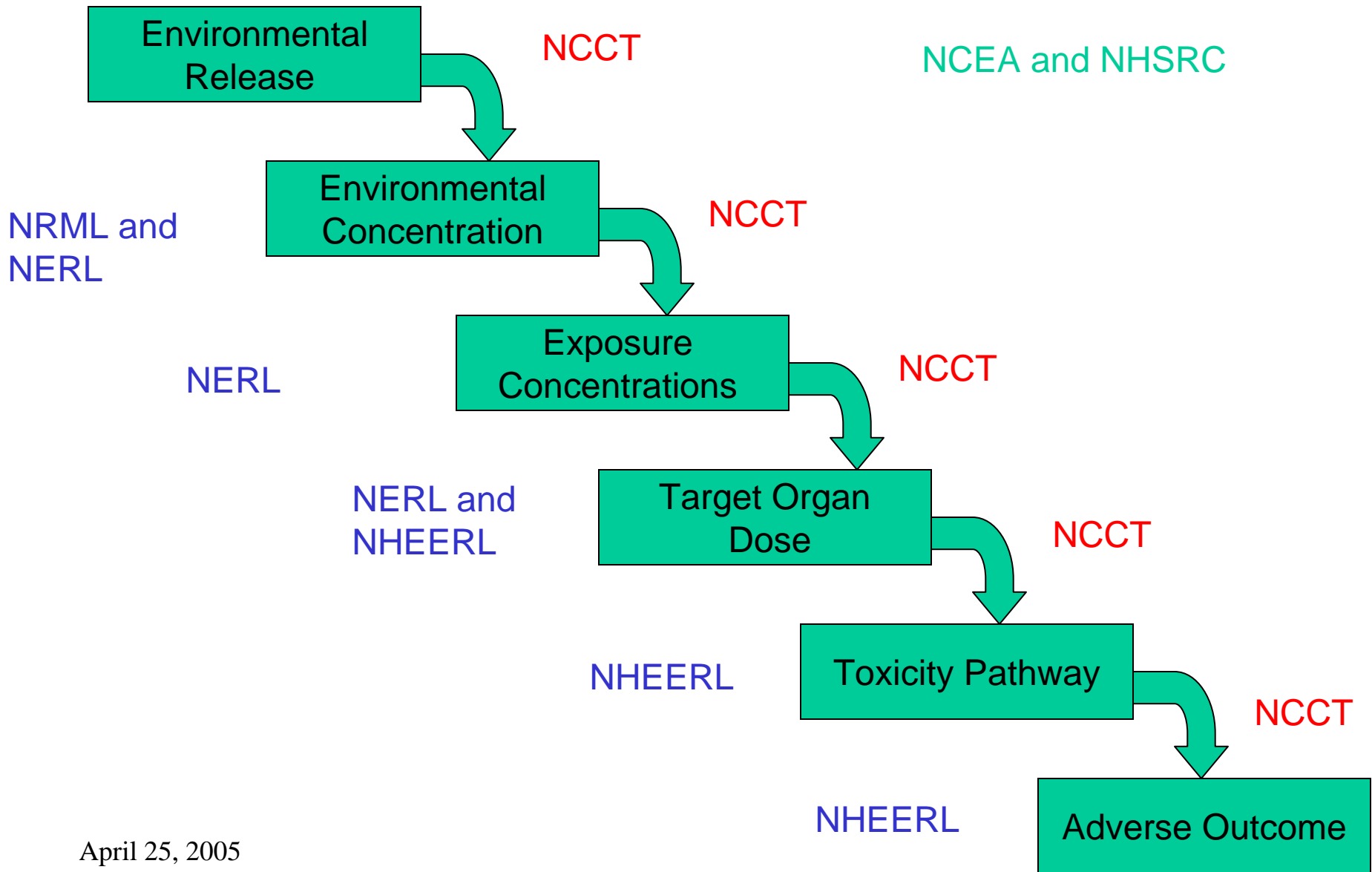
Some are "Data Generators" versus others who are "Data Users"

Computational/Omic Research

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Four Major Areas for Center

- Informatics
- Prioritization
- Systems Modeling
- Cumulative Risk Assessment

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Interactions - Informatics

- Informatics spreads across several areas in the source to outcome continuum
 - SAR with toxic endpoints
 - Computational chemistry to help provide in-silico derived parameters to exposure, biological DR, and systems models

Interactions - Informatics

- Databases to associate structure with endpoints
- Databases to organize, characterize, and analyze the “omics” information
- Databases derived from unstructured data
 - IBM demo at Science Forum in May

Interactions - Informatics

- Two labs and NCCT have or will have informatics experts to handle “omics” information
 - Working or steering group
- NCCT’s senior informatics expert to interact with STAR informatics grantee through cooperative agreement

Interactions - Informatics

- SAR and computational chemistry scientists work:
 - With informatics experts to connect structure with toxic endpoints, “omics” information, and physical properties
 - Impacted include NHEERL and NERL
 - With exposure, dose-response, and systems modelers to develop key governing parameters for models
 - Modelers are in NCCT, NHEERL, NCEA, and NERL, NIEHS, and elsewhere

Interactions - Prioritization

- Predictive models and methods for screening and testing
 - NCCT working on this and planning new hires during this year
 - Several on-going projects in NHEERL deal with this – NCCT will work to coordinate
 - “New starts” – NCCT funding to labs and centers
 - NCCT will be involved in cooperation with outside groups for several areas of computational toxicology including prioritization areas

Interactions - Systems Biology

- “...systems biology helps to make the linkages in the source to dose to outcome continuum
 - Harnesses the power of mathematics, engineering, and computer science to analyze and integrate data on understanding normal physiology to elucidate the mechanisms of the “abnormal”

Interactions – Systems Biology

- Some “systems”
 - Key molecular pathways of functioning cells
 - Interaction of cells of a tissue
 - Organ systems
 - Morphogenesis
 - Whole organism
 - Ecosystems
 - Exposure dose response continuum

Interactions – Systems Biology

- Expert modelers located in all labs and centers
 - NHEERL, NCEA and NCCT
 - Biologically based dose response
 - Physiologically based pharmacokinetic
 - Pharmacodynamic and systems
 - NERL
 - Fate and transport
 - Source to receptor
 - Exposure
 - Physiologically based pharmacokinetic
 - Pharmacodynamic
 - NRML
 - Fate and transport
 - Source to receptor
 - Exposure

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Interactions – Systems Biology

- Numerous projects within other labs and centers that NCCT can contribute additionally to develop systems biology approaches
 - NHEERL/NERL/NCEA/OPP project on cumulative risk from pyrethroids
 - NERL and NHEERL children's exposure and risk projects

Specific Mechanisms for Collaboration

- NCCT staff came from NERL and NHEERL so we have natural connections
- “New Starts”
 - All within other labs and centers
- CTISC

Specific Mechanisms for Collaboration

- New ST hired (May 2005) is an expert systems modeler
 - Will help design research program in modeling and QRA and coordinate with labs and centers and with outside scientists
- Cross ORD modeling workgroup
 - Regular communication and sharing of ideas and work loads

Specific Mechanisms for Collaboration

- Cross ORD working group of bioinformatics specialists – create synergy and avoid “reinventing the wheel”
- Regular scientist to scientist meetings with other lab and centers and with NIEHS – identify and implement joint projects of interest
- Connection with STAR program

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Specific Mechanisms for Collaboration

- Adjuncts
 - Staff from other labs and serve on detail to center to work on particular projects
- Associates
 - Staff from other labs who work on projects related to computational toxicology or have a direct interest serve informally with the NCCT staff
 - We already have one such arrangement
- Agency Risk Assessment Forum
 - Two NCCT staff are members
 - Others serve on Forum Workgroups