Design and Evaluation of ExO:
An Ontology for Exposure Science

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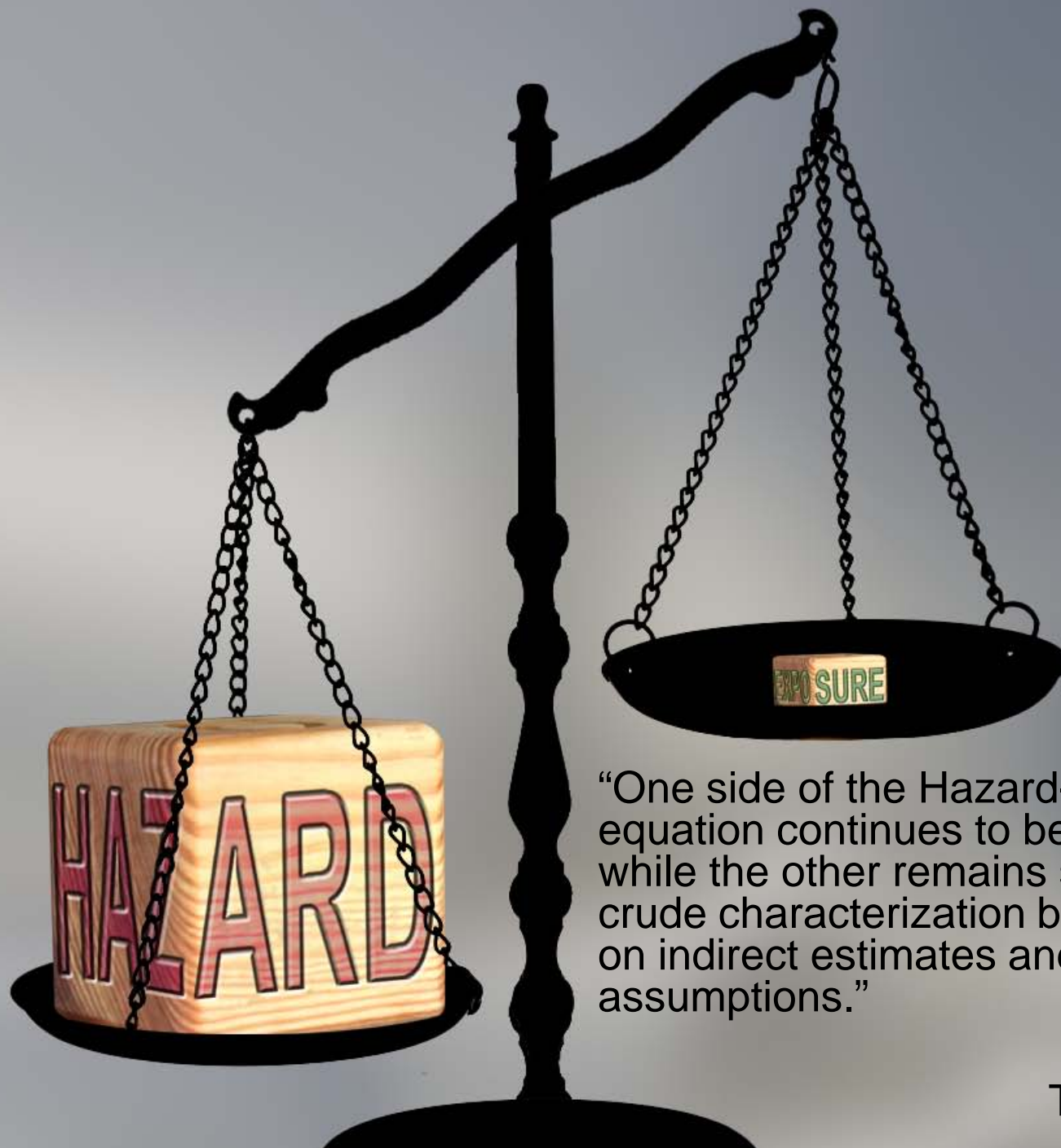
"One side of the Hazard-Exposure equation continues to be refined while the other remains subject to crude characterization based largely on indirect estimates and default assumptions."

Tox Sci 2009

**United States
Environmental Protection
Agency**

Will fundamental knowledge of toxicity pathways improve understanding of real-world human-health risk?

- Assessing complex human-health risks requires that **hazard**, **susceptibility**, and **exposure** are all reliably characterized.

- Currently, balance of efforts to improve measuring hazard and exposure less than ideal.

- Accurate assessment of many environmental exposures remains an outstanding and largely unmet challenge in toxicology and risk assessment.

- **To realize the NRC vision for toxicity testing, we face a critical need for advanced exposure science.**

Transforming Exposure Science for Toxicity Testing

New technologies must be applied to *BOTH* toxicology and exposure science if the ultimate goal of evaluating chemical safety is to be achieved.

- **Systems exposure science**

- **Biologically-relevant exposure metrics**

- **Environmental informatics and advanced computational models**

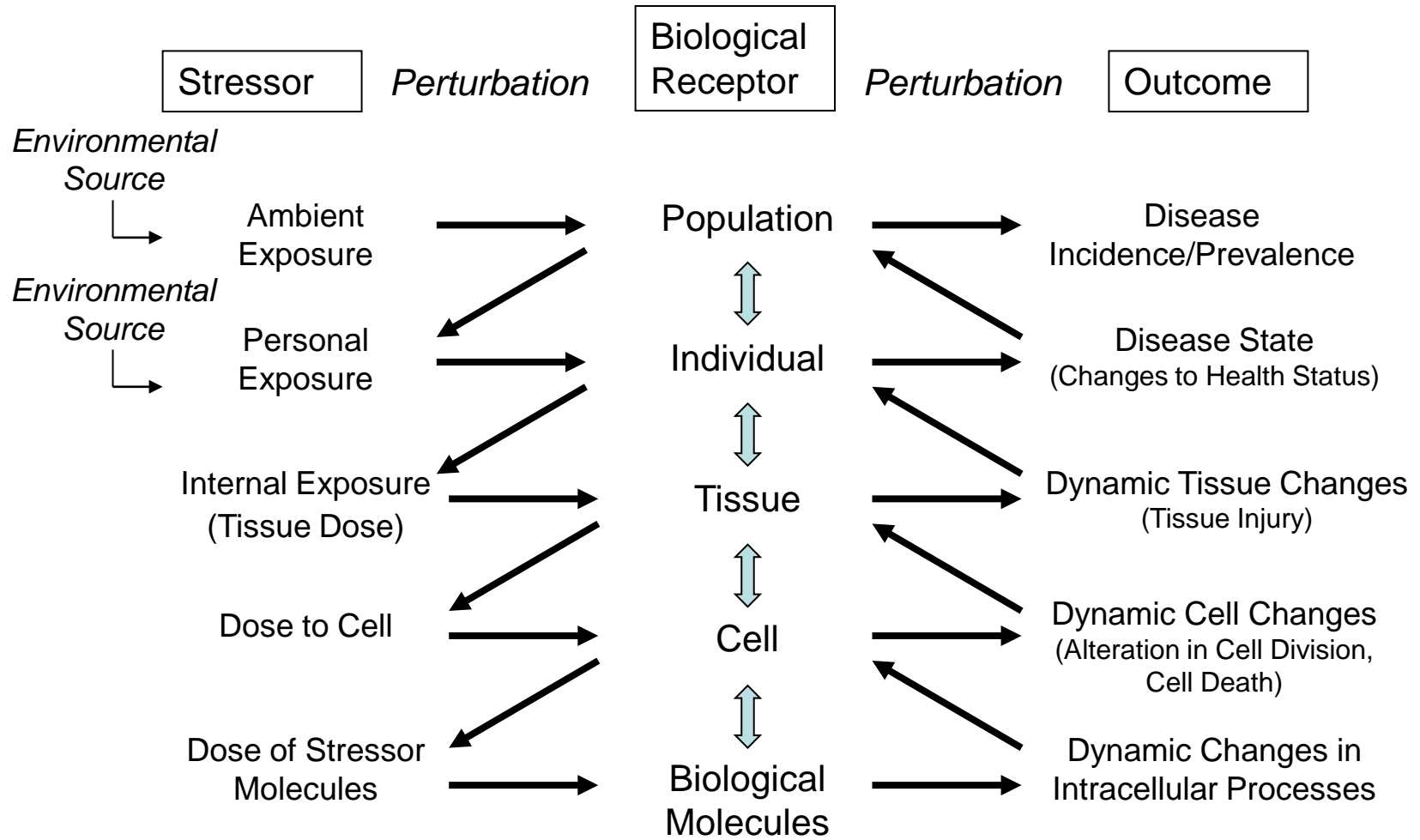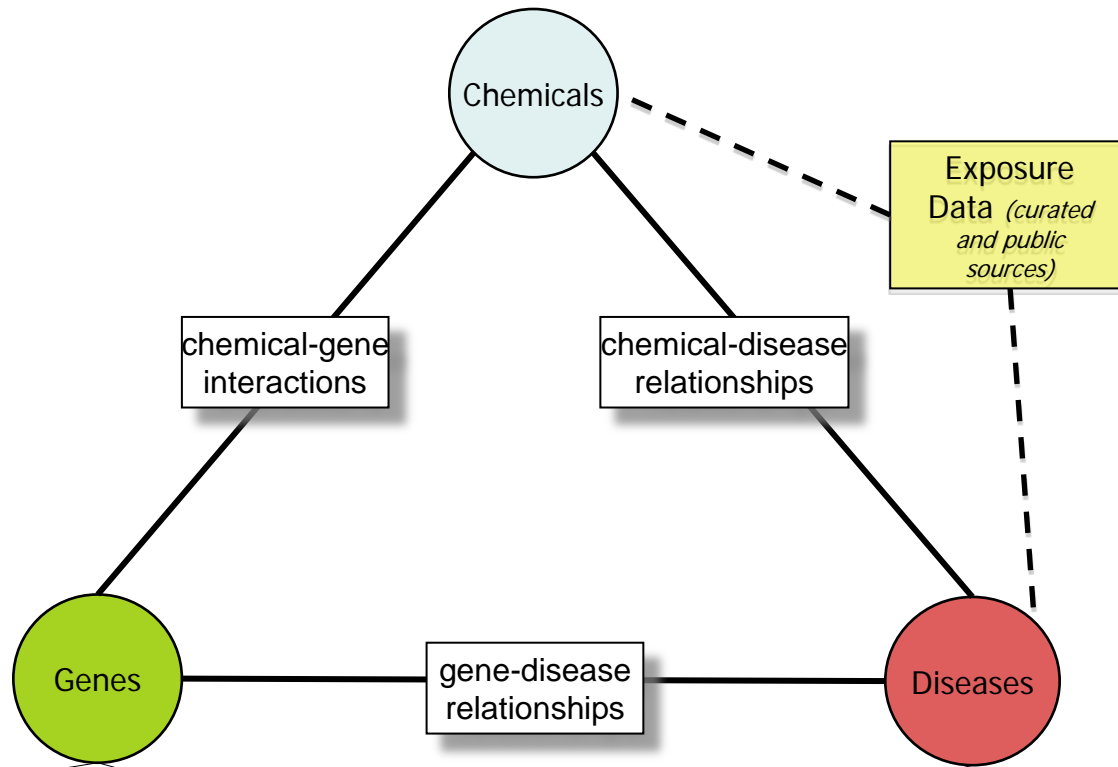Cohen Hubal, Tox Sci, 2009

Figure 1

Exposure-Hazard Knowledge System

- Translation of HTP hazard information requires holistic risk assessment knowledge system
  - Include ontologies, databases, linkages
  - Facilitate computerized collection, organization, and retrieval of exposure, hazard, and susceptibility information

- Standardized exposure ontologies required to
  - Define relationships, allow automated reasoning, facilitate meta analyses
  - Develop biologically-relevant exposure metrics
  - Design *in vitro* toxicity tests to measure environmentally-relevant hazard
  - Incorporate information on susceptibility and background exposures to individual and population-level risks

Pilot Curation of Exposure Data into Comparative Toxicogenomic Database

Chemicals

chemical-gene interactions

chemical-disease relationships

Exposure Data *(curated and public sources)*

Genes

gene-disease relationships

Diseases

the Gene Ontology

functional annotations

pathway data

Davis et al., 2011

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CTD advances understanding of the effects of environmental chemicals on human health.
—The—
Comparative Toxicogenomics Database™

Design and Evaluation of the Exposure Ontology: ExO

Background:

- Significant progress has been made in collecting and improving access to genomic, toxicology, and health data
- These information resources lack exposure data required to
  - translate molecular insights
  - elucidate environmental contributions to diseases
  - assess human health risks at the individual and population levels

Objective:

- ExO, that will facilitate centralization and integration of exposure data to inform understanding of environmental health
- ExO is intended to bridge the gap between exposure science and environmental health disciplines

Vehicle:

- Carolyn Mattingly, Mount Desert Island Biological Laboratory
- LRI seed funding, followed by NIEHS RO1

Objective

- Develop an exposure ontology consistent with those being used in toxicology and other health sciences to support annotation of **the outcome of exposure of a receptor (human or ecological) to a stressor (chemical, biological, physical, psychosocial).**

- Initially focus development on human exposure to chemicals

- Ultimately, provide domains that can be extended to encompass exposure data for the full range of receptors and stressors.

Exposure Ontology Working Group

| Working Group Member	Institution	Role/expertise
Carolyn Mattingly, PhD	Mount Desert Island Biological Laboratory	Facilitator/curated database development
Judith Blake, PhD.	The Jackson Laboratory	Facilitator/ontology development
Michael Callahan, PhM.	MDB, Inc.	Core Member/ exposure assessment
Elaine Cohen Hubal, PhD	US EPA; NCCT	Core Member/ exposure research
Robin Dodson, ScD.	Silent Spring Institute (SSI)	Member/exposure research
Peter Egeghy, PhD.	US EPA, NERL	Member/exposure research
Jane Hoppin, ScD.	NIEHS	Member/epidemiology
Thomas McKone, PhD.	Lawrence Berkeley National Laboratory (LBNL)	Core Member/ exposure research
Ruthann Rudel, MS.	Silent Spring Institute (SSI)	Member/exposure research

Phases of Exposure Ontology Development

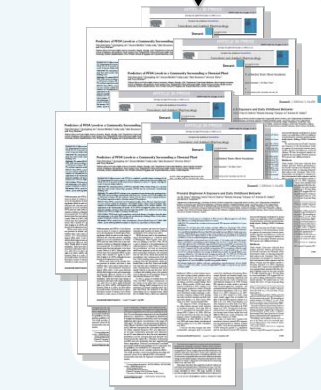**Phase I**

Phase II

Phase III

Phase IV

Initial pilot curation to identify major concepts
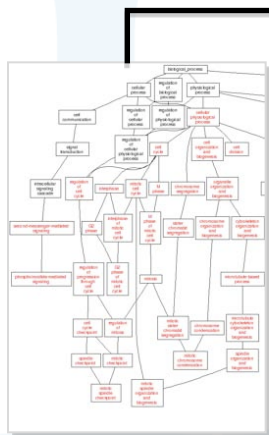
Model relationships among data concepts

Expand test data set to evaluate extensibility of conceptual model and cross-reference existing ontologies

Iterate data model refinement and curation

Full working group evaluation of draft ontology

Disseminate exposure ontology for public feedback

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Central Concepts Frame Exposure Ontology

Stressor

Receptor
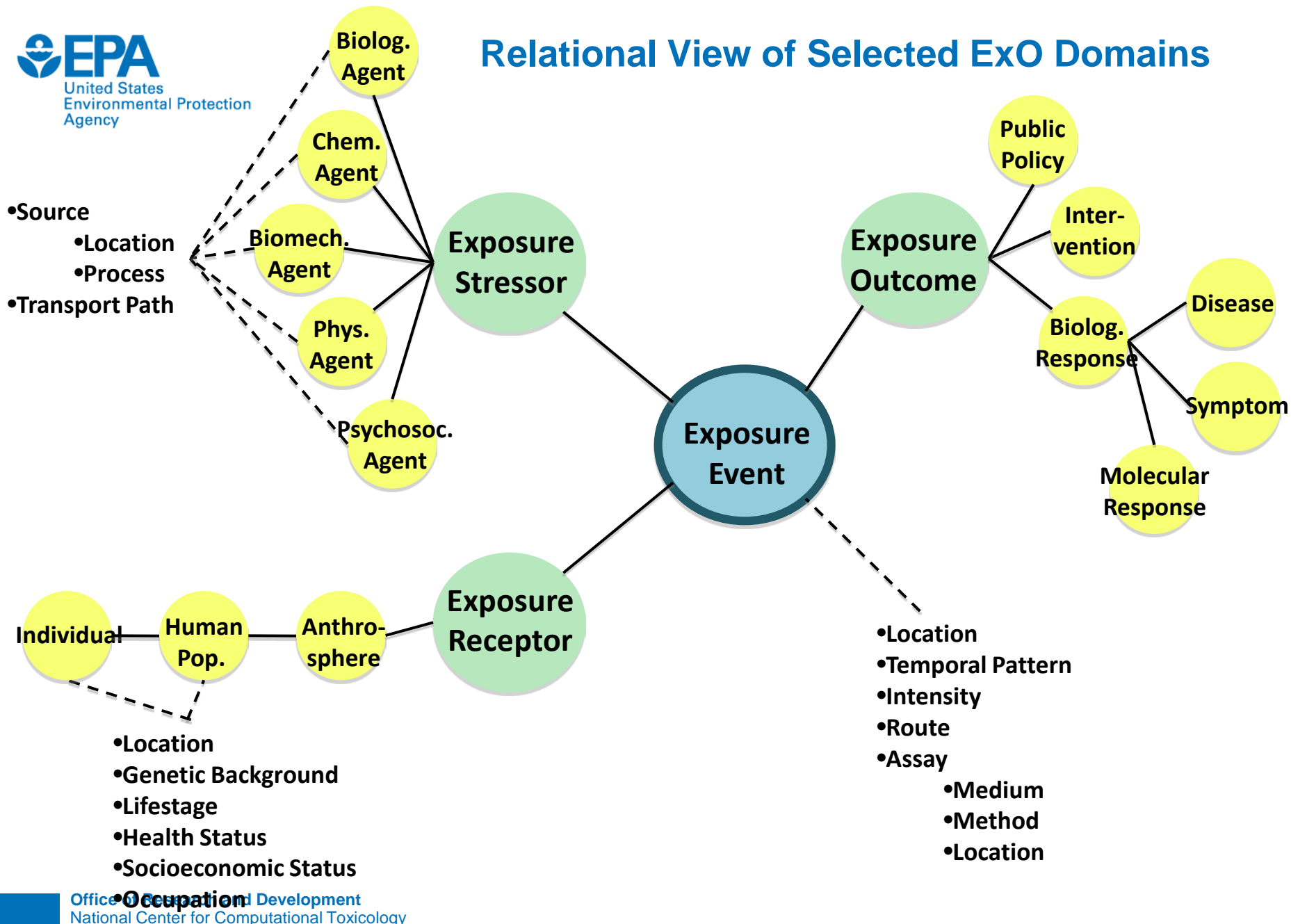
Exposure
(Location, Time)
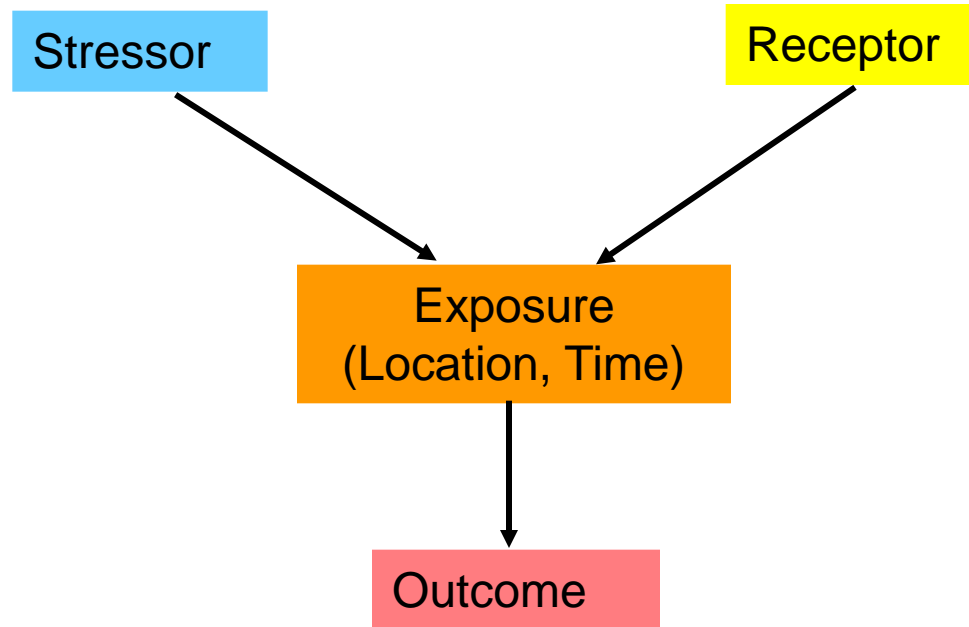
Outcome

"stressor interacts with a receptor via an exposure event resulting in an outcome"
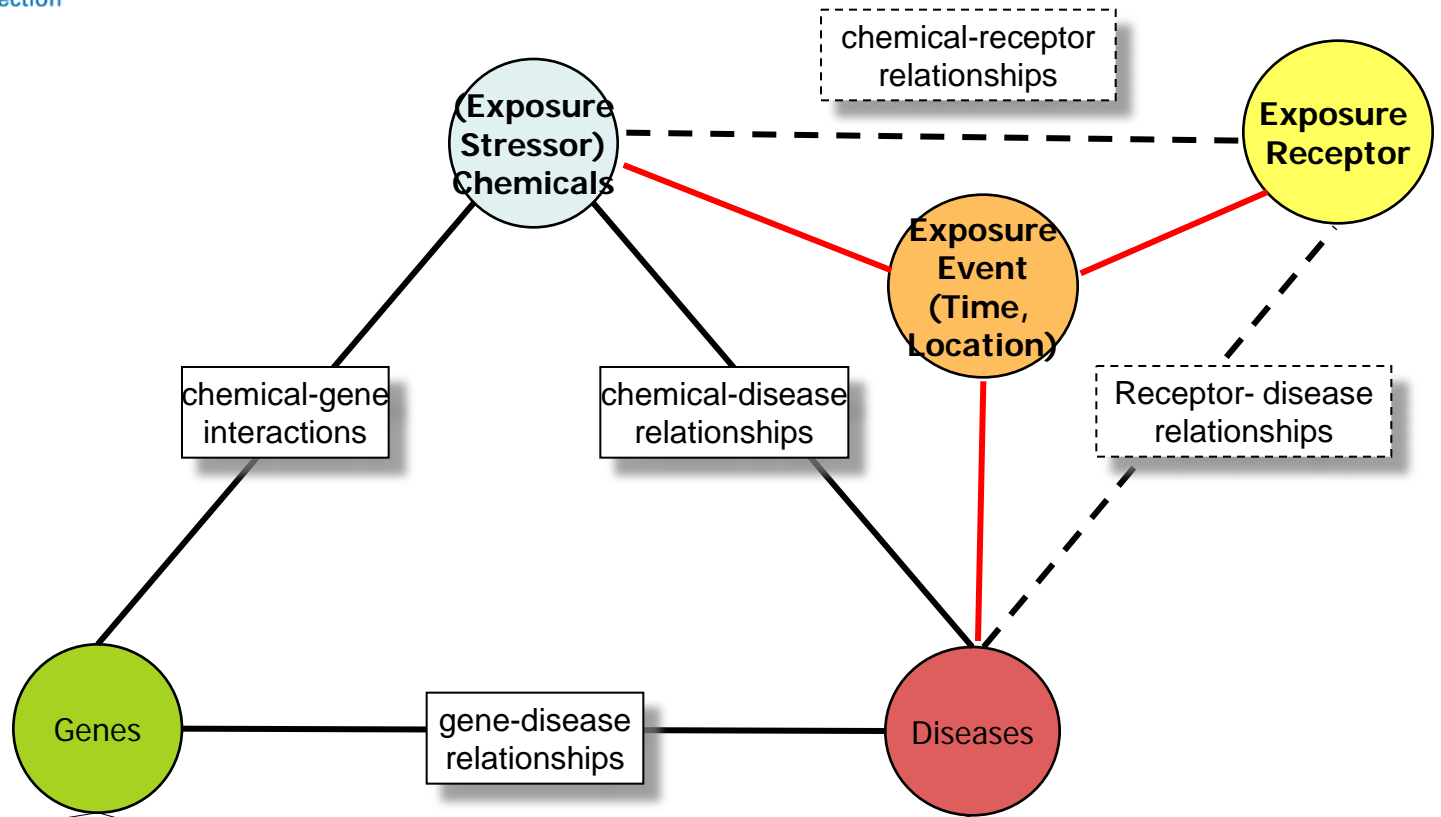
Definitions of Central Concepts

- **Exposure Stressor** - An agent, stimulus, activity, or event that causes stress or tension on an organism (UMLS Cui:C0597530).

- **Exposure Receptor** - An entity (e.g., a human, human population, or a human organ) that receives a stimuli (e.g., environmental exposure).

- **Exposure Event** - Contact between a stressor and a receptor.
- ("An exposure event is the act of subjecting someone or something to an influencing experience. E.g. exposure to cigarette smoke." [EFO:0000487])

- **Exposure Outcome** - Entity that results from the interaction between other entities (SBO:0000409)

Relational View of Selected ExO Domains

Pilot Curation of Exposure Data into CTD

United States Environmental Protection Agency

chemical-receptor relationships

(Exposure Stressor) Chemicals

Exposure Receptor

Exposure Event (Time, Location)

chemical-gene interactions

chemical-disease relationships

Receptor- disease relationships

Genes

gene-disease relationships

Diseases

the Gene Ontology

functional annotations

pathway data

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CTD advances understanding of the effects of environmental chemicals on human health.

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