

## The Environmental Conditions, Treatments, and Exposures Ontology (ECTO): Connecting Toxicology and Exposure to Health and Beyond



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- 1) What is ECTO & where's the need
- 2) Current exposure content
- 3) Contributing to ECTO
- 4) Use cases
- 5) Future Directions

# What is ECTO?

- **E**nvironmental
- Conditions
- **T**reatments

and exposures Ontology ECTO is focused on creating content related to both natural and experimental exposures including experimental treatments and usual or new environmental conditions that can be experienced by organisms

## Current environmental health resources



- Content ranges from wet lab to field research to epidemiology
- Most all resources have limited use of standardized language and do not offer a computational structure to support integration of heterogeneous data types

## Exposure content in ontologies

Entities that organisms are exposed to

- Environmental materials
- Foods
- Chemicals
- Mixtures

Positive or negative health outcomes of the exposure

- Diseases
- Phenotypes

Species specific exposure ontologies (zebrafish, plants etc.)

We are still missing the exposure event terminology...



## Exposure ontology (ExO) schema

- ExO contains a small subset of terms needed to model an 'exposure event'
- No distinct exposures are modeled in ExO (e.g., exposure to lead)
- ExO is used as the upper level schema for ECTO, using 'exposure event' as the parent term to specific exposure content



## Focused on the foundation of exposures, not specific exposures

## Modeling exposures in ECTO



Exposure events with required stimuli components and optional mediums, and routes creates defined classes in ECTO

## DOSDPs help efficiently create classes

- A majority of terms in ECTO are created using Dead Simple OWL Design Patterns (DOSDP)
- Stimulus, medium, and route can all be specifically identified in an ECTO term
- All "variables" used in ECTO terms are contained in other ontologies (e.g., ENVO, FoodOn, ChEBI)



Relationships to describe the exposure event exist, however more relationships are needed to connect organisms to exposure events

#### related via exposure (RO:0002244)

#### has exposure receptor (RO:0002240):

A broad relationship between an exposure event or process and any entity (e.g., an organism, organism population, or an organism part) that interacts with an exposure stimulus during the exposure event.

#### has exposure route (RO:0002242):

A broad relationship between an exposure event or process and a process by which the exposure stressor comes into contact with the exposure receptor

#### has exposure medium (RO:0016004):

X has exposure medium Y if X is an exposure event (process), Y is a material entity, and the stimulus for X is transmitted or carried in Y

#### has exposure stimulus (RO:0002309):

A relationship between an exposure event or process and any agent, stimulus, activity, or event that causally affects an organism and interacts with an exposure receptor during an exposure event.

#### has exposure stressor (RO:0002241):

A broad relationship between an exposure event or process and any agent, stimulus, activity, or event that causes stress or tension on an organism and interacts with an exposure receptor during an exposure event.

## Modeling exposure specifics can be tricky...

Question 1: 'Have you ever been exposed to alkalis for 15 minutes a week or more in any job you have held?' Answer: 'Yes' (Choose all that apply)

#### Sodium hydroxide

Calcium hydroxide Potassium hydroxide Magnesium hydroxide Other (specify) Question 2: 'When you were exposed to alkalis at work, how often were you exposed?' Daily **At least once per week** At least once per month At least once per year Question 3: 'What year did you start being exposed to alkalis in any job you have held?' Answer: '1983'

Question 4: 'What year did you stop being exposed to alkalis in any job you have held?' **Answer: '1987**' How much exposure actually occurred?

What is the route of exposure?

Are they wearing any PPE?

What concentration of chemical were they exposed to?



## Proposed ECTO Annotation Model (partial view)

EXAMPLE

Database	ECTO Term Label/ ID (required)	Stimulus Quantity or Concentration	Exposure Quantity	Time course	Evidence Code (required)	Citation (optional)	Creator
Database_name	'Ecto term' ECTO:0000000	UO:0000000 (units of measurement ontology)	XXX	ISO: yyyy - ISO: yyyy	ECO:00000 00	PMID:XXXXX	ORCiD
PEGS_ExpA PEGS:104	Exposure to lead in water via ingestion (ECTO:0080003)	4 mcg/L (UO:0000301)	36	ISO: 2015 - ISO: 2016			https://orcid .org/0000-0 002-7463-6 306



Let's delve into some use cases...

# Harmonizing survey questions to increase power and connectivity



- Survey questions on nutrition and environmental exposures
- Topical areas for each question can be identified and assigned to a relevant ontology term

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Given the embedded 'milk' term from FoodOn contained within the ECTO term, we can connect to other resources that use FoodOn IDs, including the USDA Food Data Central Composite exposures and mixtures connect between ontologies

- Exposure to mixture substances requires the mixture term referenced to include all components
- In turn, all components of the mixture are referenced as part of the exposure



Coordinating survey responses can connect between surveys and across ontology aligned data



## Humans create error, which can impact data quality

- Zebrafish researchers from across a variety of laboratories were asked to assess images of zebrafish larvae for morphological malformations in 2 surveys:
  - One which the researcher used their own terminology to annotate the image
  - The second contained Zebrafish Phenotype Ontology terms and definitions to be used for the annotations
- Survey responses were assessed for consistency and repeatability of image rating across participants



# Improving accuracy of human generated data through ontologies

 Utilizing ontology terms to classify exposures and phenotypic outcomes for zebrafish can offer unique inferences at higher level exposure classes or phenotypic categories



## Future directions for ECTO...

- Requests have been submitted for complex mixtures such as those focused on human conditions and multi-layered exposures (e.g., exposure to UV radiation while wearing SPF 30)
- Continuing to request new terms as needed from other ontologies to keep growing ECTO
- ECTO has the capacity to support inferences about exposures and health and can connect into existing resources like the Monarch Initiative KG, so we hope to explore those opportunities in the coming year

# Our Amazing ECTO Team!

### **Monarch Initiative**

Anne Thessen Nico Matentzoglu **Bill Duncan** Nicole Vasilevsky Julie McMurry Chris Mungall Peter Robinson Melissa Haendel

### **NIEHS**

**Charles Schmitt** 

**NC State** 

Cynthia Grondin

**CTD - ExO Team** 

Undiagnosed Disease Network

**Tanguay Lab** 

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Contact me!

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Check out our repo:

https://github.com/EnvironmentOntology/environmental-expos ure-ontology

Read our pre-print: https://doi.org/10.5281/zenodo.6360645