NTP
National Toxicology Program

Systematic Evaluation of the Application of Zebrafish in Toxicology (SEAZIT): Current and Proposed Activities

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Phase 2- In development (FY17)

- Develop protocol for assessing impact of specific identified protocol elements at several test sites
  - Impact of chorion
  - Exposure paradigm: Repeat dosing vs single
  - Use outputs to establish harmonized “approach” for Phase 3
- Development and procurement of a~30-chemical test set
- Ontologies and integration of data streams
  - Implementation of Zebrafish Ontologies for Toxicology Screening
    - Information gathering session planned for April 2017
    - Participants will discuss how to improve zebrafish screening data analysis using ontologies (standardized nomenclature).
  - Webinar series (Feb-Mar 2017) prior to the workshop

Using Informatics to Improve Data Analysis of Chemical Screening Assays Conducted in Zebrafish

- http://ntp.niehs.nih.gov/go/zfweb-2017
- Webinar 1 (February 2): Introduction to Zebrafish Screening
  - This webinar will provide an overview of the SEAZIT program and review the variability found in zebrafish screening data
- Webinar 2 (February 16): Ontologies 101
  - This webinar will define ontologies and describe how they are employed to improve data analysis
- Webinar 3 (March 2): A Review of Relevant Ontologies and Application of Reasoners
  - This webinar will provide information on relevant zebrafish, phenotype, and anatomy ontologies and provide an example of the application of ontologies and reasoners.

- All webinars will begin at 11:30 a.m. EST.

- Activities include:
  - Small group use case analysis
  - Defining data queries
  - Computing inferences via ontologies: reasoners and specific software
- Goal: Outline a recommendation document that captures best practices in data production, use, tool development, and needs to advance zebrafish applications in toxicology. A working group will be defined to continue working on the recommendations which will be presented at the Best Practices Workshop.

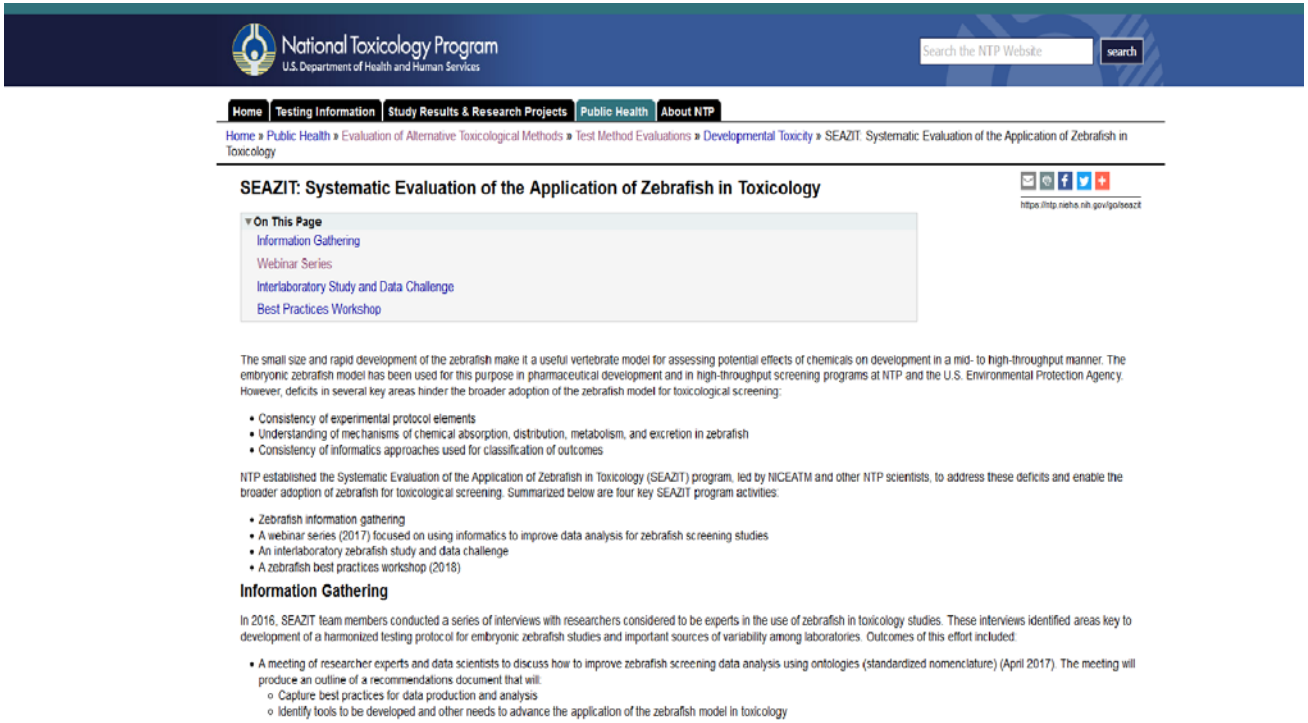
Tentatively planned for fall 2018

- Public forum to discuss continued development and standardization of assays, as well as practices for collecting, analyzing, and reporting of data.
- Objectives :
  - Identify best practices for conducting zebrafish screening assays
  - Define the state of the science for data analysis of zebrafish screening assays and develop guidelines for analyzing and reporting data
  - Define minimum essential endpoints for zebrafish screening assays
  - Develop common terminology for endpoints and effect phenotypes in zebrafish screening assays.
- The workshop will result in a recommendations document for the conduct and reporting of zebrafish screening assays to be published in the peer-reviewed literature.

Outreach 1

- Create outreach to individuals with an interest in zebrafish model development

  https://ntp.niehs.nih.gov/pubhealth/evalatm/test-method-evaluations/dev-tox/seazit/index.html



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SEAZIT: Systematic Evaluation of the Application of Zebrafish in Toxicology

https://ntp.niehs.nih.gov/go/seazit

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The small size and rapid development of the zebrafish make it a useful vertebrate model for assessing potential effects of chemicals on development in a mid- to high-throughput manner. The embryonic zebrafish model has been used for this purpose in pharmaceutical development and in high-throughput screening programs at NTP and the U.S. Environmental Protection Agency. However, deficits in several key areas hinder the broader adoption of the zebrafish model for toxicological screening:

- Consistency of experimental protocol elements
- Understanding of mechanisms of chemical absorption, distribution, metabolism, and excretion in zebrafish
- Consistency of informatics approaches used for classification of outcomes

NTP established the Systematic Evaluation of the Application of Zebrafish in Toxicology (SEAZIT) program, led by NICEATM and other NTP scientists, to address these deficits and enable the broader adoption of zebrafish for toxicological screening. Summarized below are four key SEAZIT program activities:

- Zebrafish information gathering
- A webinar series (2017) focused on using informatics to improve data analysis for zebrafish screening studies
- An interlaboratory zebrafish study and data challenge
- A zebrafish best practices workshop (2018)

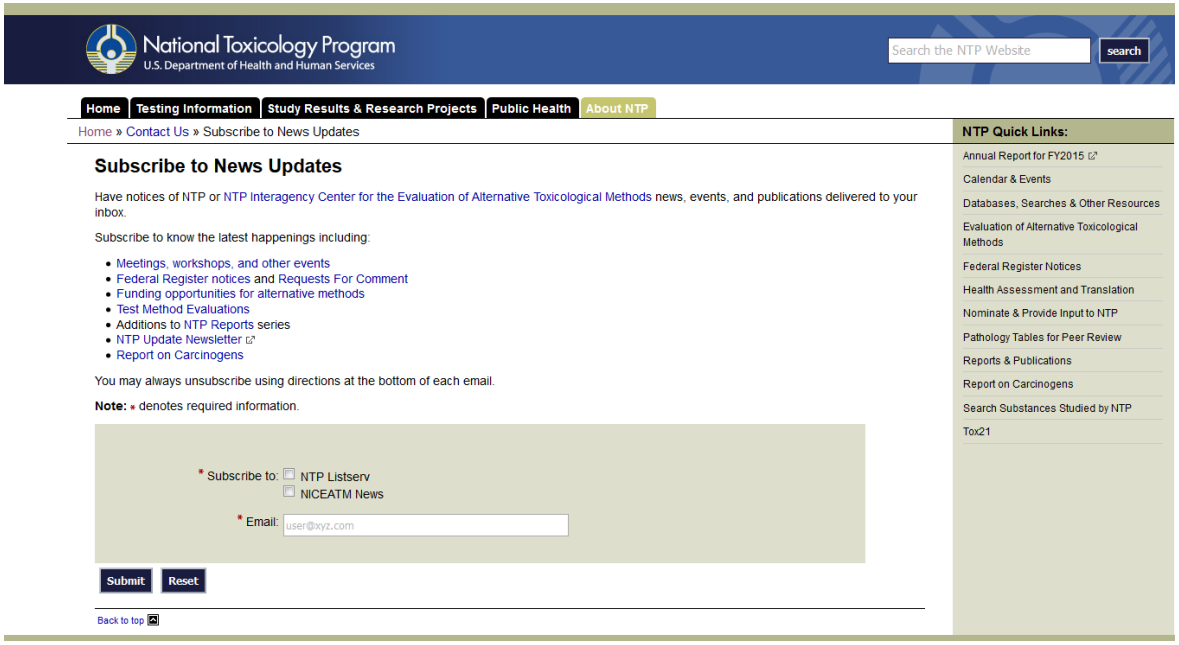
Information Gathering

In 2016, SEAZIT team members conducted a series of interviews with researchers considered to be experts in the use of zebrafish in toxicology studies. These interviews identified areas key to development of a harmonized testing protocol for embryonic zebrafish studies and important sources of variability among laboratories. Outcomes of this effort included:

- A meeting of researcher experts and data scientists to discuss how to improve zebrafish screening data analysis using ontologies (standardized nomenclature) (April 2017). The meeting will produce an outline of a recommendations document that will:
  - Capture best practices for data production and analysis
  - Identify tools to be developed and other needs to advance the application of the zebrafish model in toxicology

Outreach 2

- Sign up for updates through the NICEATM News
  - To register for the NICEATM News email list, go to: https://tools.niehs.nih.gov/webforms/index.cfm/main/formViewer/form_id/361
  - check the box to subscribe to NICEATM News



Outreach 3

- Contacts will be provided with information on:
  - Publication of the information group summary report
  - Outcomes of the ontology information session
  - Updates on the Best Practices Workshop

Feedback

- NICEATM published a Request for Information at the end of 2016
- https://ntp.niehs.nih.gov/pubhealth/evalatm/test-method-evaluations/dev-tox/nonanimal/index.html
- Requesting information on:
  - Zebrafish model development efforts
  - Data on protocol elements that influence toxicity measurements
  - Toxicokinetic data

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