

Oligonucleotide Toxicity Open Data Challenge

OligoTox Challenge



National Center
for Advancing
Translational Sciences

Agenda

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OligoTox Challenge Background

Oligonucleotide (“oligos”) therapeutics are an emerging therapeutic modality with increasing numbers of drugs in development and several approved for use in the treatment of rare genetic diseases.

Both the FDA and NIH are interested in **new approach methodologies** that can reduce the use of animal testing in preclinical safety studies such as through technologies like organoids, which are small, lab-grown tissue models that replicate the structure and function of human organs.

In recent years, we have also witnessed dramatic increases in the **use of advanced computational methods** to address complex biological problems.



OligoTox Challenge Background (cont'd)

The Challenge: NCATS seeks to incentivize the generation of **high-quality and publicly accessible open datasets** that make use of in vitro human systems and can be used to advance predictive models for oligo toxicity.

Toxicities of particular interest include hepatotoxicity, nephrotoxicity, thrombocytopenia, complement activation, coagulopathy, immunotoxicity, chronic neurotoxicity, and hydrocephalus.



Schedule, Prizes, Submitting

Phase 1: Ideation

Start: **December 19, 2025**

Submission Deadline: **February 28, 2026**

Aim: **Propose how you will collect, build, or contribute dataset from in vitro human-based systems that can be used to support the development and training of in silico models to accurately predict toxicity for a candidate oligo therapeutic**

Prizes: **Maximum of ten winners with a prize of up to \$10,000 each**

Phase 2: Data Generation

Start: **May 1, 2026**

Submission Deadline: **December 31, 2026**

Aim: **Make publicly available a high-quality open dataset with demonstratable use in developing and training predictive models for oligonucleotide toxicity**

Prizes: **Maximum of two winners with a prize of up to \$100,000 each and four runners-up with a prize of up to \$50,000 each**



Schedule, Prizes, Submitting (cont'd)

Submission Requirements for Phase 1 (selection; please refer to listing)

- A description of **how the proposed dataset would be collected, generated, or provided** (e.g., the intended source(s) for the dataset) and the **suitability of this dataset for use** in this challenge (e.g., data ownership, data use or data sharing restrictions, etc.)
- A definition of the **indicators and predictor variables** (e.g., oligo sequence, chemical modifications, etc.) **used for evaluating oligo toxicity**, and **evidence/reference(s) supporting how these indicators would reliably and validly predict toxicity** in relation to these predictor variables
- A description of the new dataset to be generated, which should include:
 - **Model system(s) to be used**, i.e., in vitro (cell culture, microphysiological system, 3-D human organoids)
 - **Toxicology readout(s) to be assessed** (e.g., cell death, changes in gene expression, etc.)
 - **Estimated number of oligos to be evaluated**, including different chemical modifications
 - **Positive and negative control oligos** and the rationale for selecting them
 - **Methods to be used for purifying oligos**, and assessing identity and purity (e.g., mass spec, HPLC, etc.)
 - **Oligo concentrations** (in vitro assays) **or doses** (in vivo experiments)
 - **Number of replicates**



Evaluation and Judging

Entries that comply with eligibility and submission requirements will be scored for scientific value, experimental approach and design, data translatability, and proposed dataset management.

A **Judging Panel**, that will include Federal employees from NIH and other government agencies, will determine winners by assigning confidence ratings on how well submitters address these **four factors**:

Ability to Solve the Challenge - Appropriateness in advancing predictive modeling of oligo toxicity

Potential Impact - Ability for the dataset to address important information gap(s)

Feasibility and Rigor - Viability and quality of this dataset

Transparency and Reproducibility - Adherence to NIH scientific data sharing policies and best practices



Q&A

Important Dates:

- **Phase 1 Submission Start/End: Dec. 19, 2025 to February 28, 2026**
- Phase 1 Winner(s) Announced: April 30, 2026

- Phase 2 Informational Webinar (Tentative): May 15, 2026
- Phase 2 Submission Start/End: May 1, 2026 to December 31, 2026
- Phase 2 Winner(s) Announced : March 15, 2027

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OligoTox Challenge

Learn more at ncats.nih.gov/funding/challenges
Questions can be sent to: ncatsoligotox@mail.nih.gov



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