NIH Venture Program *Newborn Screening by Whole-Genome Sequencing Collaboratory* (*NBSxWGS*) Initiative

Research Opportunity Announcement: OTA-25-004 Technical Assistance Webinar

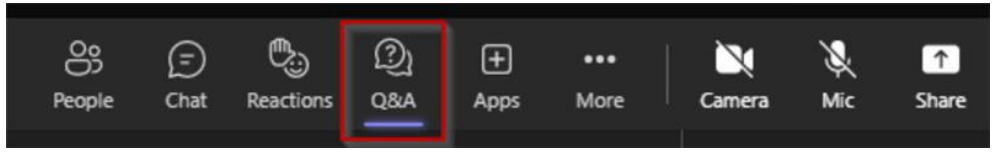
March 24, 2025

NBSxWGS Initiative Working Group

National Institutes of Health
Office of Strategic Coordination–The Common Fund

Agenda

- Overview of the Common Fund Venture Program
- Overview of the NBSxWGS Initiative Research Opportunity Announcement (ROA)
- Questions & Answers



FAQs posted at https://commonfund.nih.gov/venture/nbsxwgs/faqs

(A recording of this webinar, incl. Q&A, also will be posted to the website.)

Overview of the Common Fund Venture Program

The Common Fund Moves the NIH Mission Forward – Faster

Supports bold scientific programs that **catalyze discovery** across all biomedical and behavioral research

Advances areas of biomedical and behavioral research important to the missions of multiple NIH Institutes and Centers

Spurs subsequent biomedical advances that otherwise would not be possible without an initial strategic investment

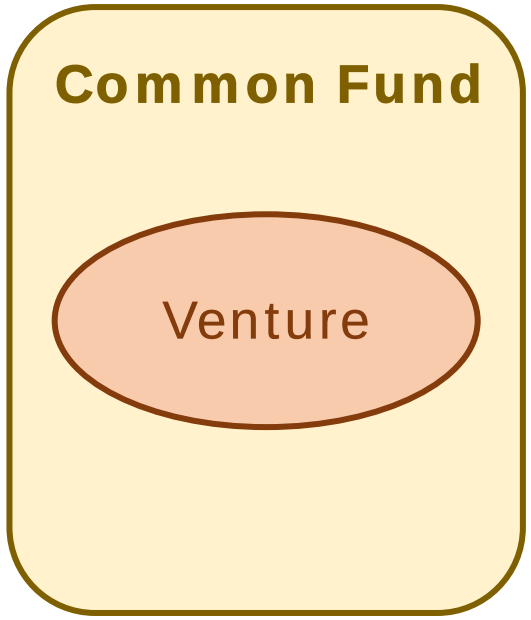
Common Fund Venture Program

"Amazing things with modest funding"

- The Venture Program makes Common Fund support available for short-term initiatives that embrace scientific risk.
- The ICO Director Venture Board prioritizes initiatives, with final approval by the NIH Director.

Common Fund Criteria:

- Transformative
- Catalytic
- Goal-driven
- Synergistic
- Novel



Venture is part of the Common Fund, not a separate activity.

Venture Criteria:

- Bold
- Nimble
- Focused

Overview of the NBSxWGS Initiative Research Opportunity Announcement (ROA)

New Venture Initiative: NBSxWGS Collaboratory

Objective: The NBSxWGS Collaboratory aims to demonstrate the feasibility of a collaborative model for NBS by WGS across multiple states, which could provide a roadmap to a national newborn genetic screening program.

Goals:

- Support centralized analysis and interpretation of WGS results for 5-10 state public health labs.
- Enable broad access to WGS as a screening tool in the newborn period.
- Focus on a limited gene panel of serious rare diseases with early treatment options available.
- Examine ethical, legal, and social implications (ELSI) of population-wide WGS in the newborn period.

Award Budget and Duration: **$4.8M TC per year** for **one** meritorious Other Transaction Award (contingent upon funding availability); maximum of a **3-year project period**

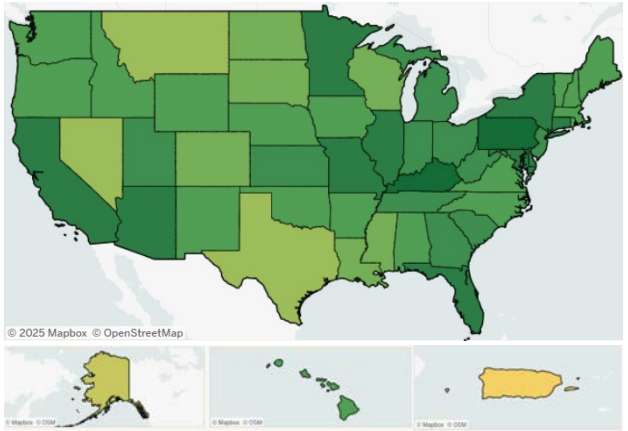
New Venture Initiative: NBSxWGS Collaboratory

Background and Goals:

- ❑ 97% of newborns in the U.S. are screened by state public health labs (PHLs).
- ❑ Most screening is done via biochemical assays on dried blood spots (DBSs) rather than DNA sequencing.
- ❑ Many states screen for 38 core conditions on the federally Recommended Uniform Screening Panel (RUSP).
- ❑ Thousands of rare genetic diseases are not screened.

Core Disorders Screened

31 — 38



Last Updated: 3/3/2025

Adding WGS to existing NBS programs could achieve the following goals:

- ❑ Expand NBS to many more diseases with available treatments/interventions.
- ❑ Shorten the diagnostic odyssey for rare diseases that are added to the list.
- ❑ Improve outcomes by allowing treatments to start earlier in the disease course.
- ❑ Make NBS programs more compatible with emerging technologies (gene therapy, gene editing) by enabling rapid addition of new diseases to NBS.

This initiative will support a collaborative, multi-state model for NBS that would use WGS as a first-tier screening assay for a set of genetic conditions that are actionable in the first year of life.

Figure: Newborn Screening Technical assistance and Evaluation Program (NewSTEPs)
www.newsteps.org/resources/data-visualizations/newborn-screening-status-all-disorders

New Venture Initiative: NBSxWGS Collaboratory

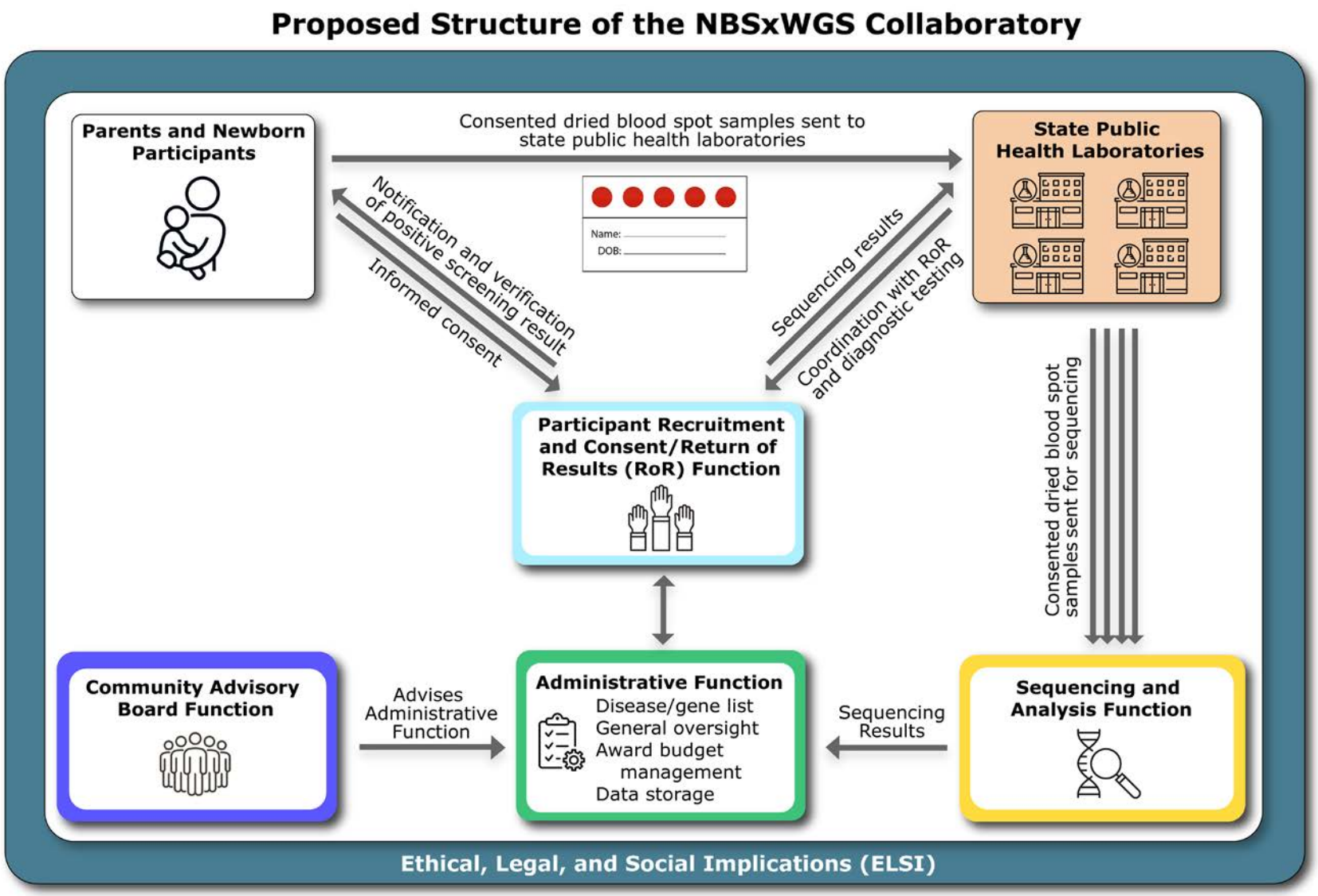


Figure: https://commonfund.nih.gov/venture/nbsxwgs

OT-25-004

https://commonfund.nih.gov/venture/nbsxwgs/funding-opportunities/OTA-25-004

Overall Purpose: To support a milestone-driven study, with significant community involvement, that will assess the feasibility of a collaborative model for incorporating WGS into the existing state-based U.S. public health newborn screening program.

- During award negotiations, the potential awardee will work with the NIH NBSxWGS Working Group to select 5–10 state PHLs from the PHL roster to participate in the project via subawards.
- The CAB will provide critical input to guide development of the informed consent process, list of genes to screen, return of results process, and genomic data sharing plan.
  - The CAB must be formed ASAP post-award (no later than by the end of Q1 in Project Year 1).

New Venture Initiative: NBSxWGS Collaboratory

Anticipated Work Products:

- **Screening of participating newborns by WGS in 5–10 states** with varying levels of experience with NIH-funded research and with WGS.
- **Embedded ELSI research study** that examines the impact of NBSxWGS on newborns and families, state NBS programs, and/or public perceptions of NBS.
- **Final report** on the feasibility of incorporating WGS into the U.S. NBS program, findings from the ELSI research study, and recommended best practices if state NBS programs decide to implement NBSxWGS.

Impact:

- If successful, this study will demonstrate the feasibility of adding WGS to an existing public health resource available to all babies born in the U.S. regardless of social, racial, ethnic, or other factors.
- The initiative will provide federal and state partners with critical data needed to inform sustained implementation of NBSxWGS.

Other Transactions

- *Not grants, cooperative agreements, or contracts*
- OTs allow the nimble addition or subtraction of expertise, tools, technologies, and partnerships.
- Many NIH policies apply to OTs, though not the traditional policies governing grants or contracts.
- Objective Reviews of applications for OTs do not follow the traditional NIH review process. The OT Team develops the criteria and composition of the review, which is designed to ensure integrity, fairness, and transparency.
- Award funding is different from typical NIH grants: variable segment lengths; no future commitment; can be terminated or extended by NIH; etc.
- Changes in project and budget are different from typical NIH grants: NIH can propose changes, threshold for prior approval, etc.

Data Management and Sharing

- Applicants are required to submit a draft Data Management and Sharing Plan (DMSP) (NOT-OD-21-013) with their application that outlines and justifies any potential limitations needed to protect the privacy and confidentiality of newborn participants.
- The final DMSP will be developed in consultation with the CAB and the NIH NBSxWGS Working Group.
- For any data that are shared according to the final DMSP, use of NIH-supported repositories (dbGaP, ClinVar) and synergies with NIH-supported studies and resources (e.g., Gabriella Miller Kids First Program, ClinGen) should be maximized to the extent possible.

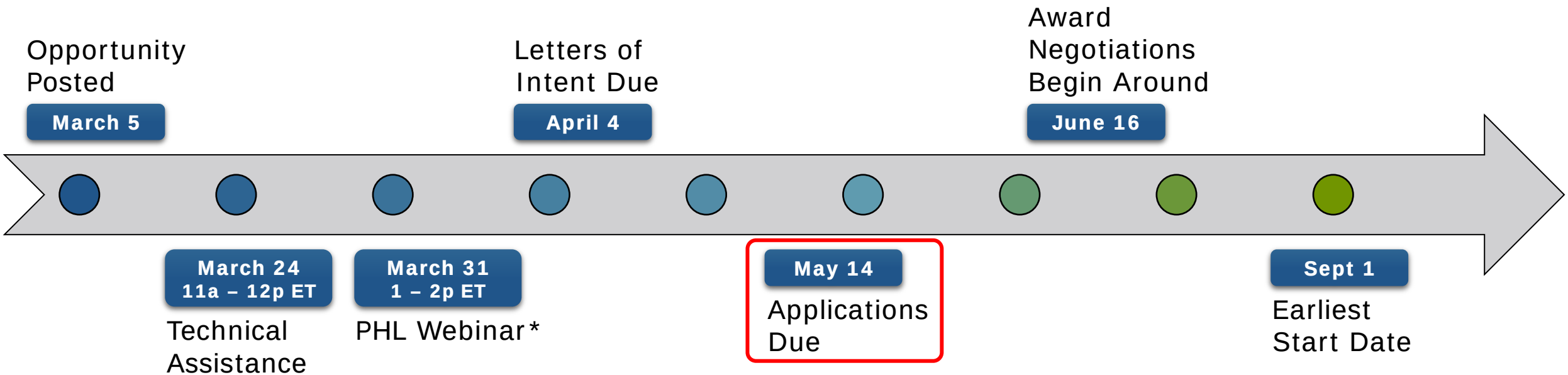
PI Eligibility and Minimum Effort Requirements

- More than one individual may be named as Principal Investigator (PI); one individual must be identified as the “Contact PI”.
- The Contact PI must be employed by or affiliated with the applicant organization.
- If a Multiple Principal Investigator (MPI) application is submitted, then an MPI leadership plan is required.
- The PI and any MPIs must collectively commit at least 20% effort to the project.
- Each Function Director must commit at least 10% effort to provide leadership for that function.

Letter of Intent (LOI)

- An LOI is **required** to be eligible to submit a full application.
- NIH will use LOIs to plan the review panel and mitigate potential COIs for prospective reviewers.
- LOIs are limited to 4 pages and must contain the following:
  - **Heading** (Title, Contact PI, Business Official, and Applicant Institution)
  - **Project Summary/Abstract** (1 page)
  - **List of All Key Personnel** (up to 3 pages total), including titles, affiliations, and roles and responsibilities on the project. As appropriate, also provide: eRA Commons IDs, prior experience in obtaining IRB and other regulatory approvals for return of genetic sequencing results, and prior history of receiving NIH and other federal awards.
- LOIs must be emailed as a PDF attachment to NBSxWGS@od.nih.gov
- LOI due date: **Friday, April 4, 2025**
- NIH will provide email confirmation of LOI receipt. The **confirmation email must be included in the "Project Information Summary" section** of the full application.

Timeline Overview



*Webinar recordings and slides will be made available on https://commonfund.nih.gov/venture/nbsxwgs

Application Due Date: Wed., May 14, 2025
by 5:00 PM local time of applicant organization

- Applications will have multiple components as listed in section 8.3 of the ROA.
- If applicable, page limits for components are stated in the ROA.
- Title the components the same way they are named in the ROA.
- **Due by 5 pm local time of applicant organization. Late applications will not be accepted.**
- Applications must be submitted electronically through ASSIST (see sections 8 of the ROA for guidance).

For additional information:

Visit the FAQ page:
https://commonfund.nih.gov/venture/NBSxWGS/faqs

Contact the Program Team:
NBSxWGS@od.nih.gov

commonfund.nih.gov

@NIH_CommonFund

National Institutes of Health
Office of Strategic Coordination–The Common Fund

Questions and Answers

Thanks for attending

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