

## Concept Clearance

**Branch:** Exposure, Response, and Technology Branch

**Council Period:** 202301

**Concept Title:** Global Exposome Research Coordination to Accelerate Precision Environmental Health

### Introduction

The exposome is defined as the totality of exposures to which an individual is subjected from conception to death, including those resulting from environmental agents, socioeconomic conditions, lifestyle, diet, and endogenous processes [1, 2, 3]. The exposome concept provides a framework for discovery of novel exposure-disease associations through more comprehensive exposure assessment in epidemiology studies and, more importantly, opportunities for better understanding the role of complex gene environment interplay in the etiology, treatment, and prevention of complex diseases such as cancer, Alzheimer's, Type 2 Diabetes, asthma, and cardiovascular disease. The study of the exposome (i.e., exposomics) has led to a paradigm shift in environmental health research in the past decade which was evidenced by major investments in exposome research around the world. These include the exposome projects funded under the EU FP7 Exposome Program (HELIX, EXPOsOMICS, HEALS), the Japan Environment and Children's Study (JECS), the establishment of Children's Health Exposure Analysis Resource (CHEAR), followed by the Human Health Exposure Analysis Resource (HHEAR), and the formation of European Human Exposome Network (EHEN) funded under Horizon 2020. Additionally, large NIH-supported initiatives are embracing the exposome concept to capture both environmental and genetic contributions in health and disease. For example, the Environmental influences on Child Health Outcomes (ECHO) Program addresses the impacts of a broad range of early environmental exposures on child health and development by taking advantage of recent technological advances including leveraging HHEAR for large scale, comprehensive exposure analyses. In FY23, the National Institute of Aging (NIA) approved a group of 4 concepts which included a focus on understanding the role of the exposome in the etiology of Alzheimer's disease and related dementias. With increased recognition and adoption of the exposome concept by the national and international biomedical research community, there is a critical need for global coordination and cooperation to build off ongoing exposomics efforts and capitalize on technological innovations in various disciplines and existing resources, just like the success of the Human Genome Project was achieved through a highly collaborative international effort.

In the summer of 2022, a series of open space workshops entitled "Accelerating Precision Environmental Health: Demonstrating the Value of the Exposome" was held by NIEHS to address challenges and opportunities in exposome research and explore paths forward [4]. The workshop series attracted more than 400 unique participants from around the globe and a wide range of topics were raised, followed by a prioritization session and a summit meeting. While numerous opportunities and research gaps were identified in various areas, including methods standardization and scale up, geospatial mapping of the exposome, creating interoperable data repositories, using AI and machine learning for data integration, and applying exposomics to address health problems at both individual and community levels, the first step to tackling these issues is to establish a community of practice to define a framework for exposome research, develop guiding principles and best practices, and leverage ongoing efforts and existing resources for operationalizing exposomics. Additionally, the 2021 NIEHS workshop "Integrating Multiscale Geospatial Environmental Data into Large Population Health Studies" also pointed to the importance of interdisciplinary collaboration (exposure science, geospatial technologies, epidemiology, genomics and genetics, and data science) and international coordination in the geospatial space [5]. In December 2022, the European Commission released a call for "Global Coordination of Exposome Research" under 2023-24 Horizon Europe, the major activities of which include 1) proposal for a commonly agreed conceptual framework for the

exposome; 2) Proposal for options for a global governance structure for a Global Human Exposome Network; 3) Agreed upon technologies needed to decipher the exposome, and more. It specifically calls out the importance of leveraging ongoing related activities in the US (National Institute for Environmental Health Sciences) and other places for global cooperation [6].

### Research Goals and Scope

This concept is to establish the US counterpart of the European “Global Coordination of Exposome Research”. The goal is to build an international community of exposome research for promoting methods and resources sharing and fostering national and international collaborations, taking advantage of existing exposome research initiatives, infrastructures, and resources. The “Global Exposome Research Coordination to Accelerate Precision Environmental Health” will engage with various groups and communities that are relevant, including the European “Global Coordination of Exposome Research”, to develop guiding principles and best practices in exposomics. **Applicants should work with the US exposome research community and international partners on the following activities:**

- ❖ **Develop a commonly agreed upon conceptual framework for exposomics.** The framework should address the following questions:
  - What are the measurable elements of the exposome in human studies based on the state of science (what should/can be measured)?
  - What is the role of animal models and in vitro systems in exposomics?
  - What are the essential technologies/methodologies for conducting exposomics?
  - What are the data standards and data infrastructure needs for supporting exposomics?
  - How to apply exposomics to advance precision environmental health at both community and individual levels?
- ❖ **Identify agreed upon technologies/methodologies needed for characterizing the exposome** to support ongoing and future exposome initiatives in the US and potentially for international cooperation, leveraging ongoing efforts and existing resources (Common Fund Metabolomics, ECHO protocols and resources, Multi-Omics for Health and Disease initiative, NIEHS data and metadata standards initiative, HHEAR, BP4NTA, EHEN). Activities include but not limited to:
  - Hold workshops and consensus meetings to develop performance standards and/or best practices for exposome data collection, analysis, and reporting (e.g., geospatial exposure modeling, untargeted exposomics, multi-omics integration, sensors, AI and machine learning).
  - Create quality control materials to facilitate cross study harmonization of exposure data; organize round-robin activities to promote inter- and intra-laboratory comparability.
  - Identify future needs in technology/methodology for data collection, analysis, and translation of results.
  - Disseminate methods, best practices, and quality control materials to the broad biomedical research community.
- ❖ **Build a global community of exposome research**, working with the European “Global Coordination of Exposome Research” and other partners. Activities include but not limited to:
  - Develop a global governance structure for a Global Human Exposome Network, taking advantage of and connecting to existing exposome research initiatives and infrastructures around the world.
  - Identify opportunities for future collaboration in data mining, harmonization and integration (including integration with genomics data), leveraging existing and ongoing efforts (e.g., TOPMed, ECHO, HHEAR, All Of Us, UK Biobank).
  - Provide education, training, and outreach and promote an exposome community of diversity and inclusion.

## Mechanism and Justification

It is anticipated that the project will build a community of exposome research through frequent outreach and consensus building activities among relevant groups and communities. Resource building is also a major goal of this project. Commonly agreed upon technologies and best practices for exposome research will be disseminated to the broad biomedical community for adoption. Thus, U24, a cooperative agreement to support research to improve the capability of resources to serve biomedical research will likely to be used. Alternatively, R24 can be considered, which supports research projects that will enhance the capability of resources to serve biomedical research.

### Reference

1. Porta, M. A Dictionary of Epidemiology. 6th edition, Oxford University Press 2014 p104
2. Wild CP. Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. *Cancer Epidemiol Biomarkers Prev.* 2005 Aug;14(8):1847-50.
3. Vermeulen R, Schymanski EL, Barabási AL, Miller GW. The exposome and health: Where chemistry meets biology. *Science.* 2020 Jan 24;367(6476):392-396.
4. <https://www.niehs.nih.gov/news/events/pastmtg/2022/exposomics2022/index.cfm>
5. Cui Y, Eccles KM, Kwok RK, Joubert BR, Messier KP, Balshaw DM. Integrating Multiscale Geospatial Environmental Data into Large Population Health Studies: Challenges and Opportunities. *Toxics.* 2022 Jul 20;10(7):403.
6. [https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/wp-call/2023-2024/wp-4-health-horizon-2023-2024\\_en.pdf](https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/wp-call/2023-2024/wp-4-health-horizon-2023-2024_en.pdf)