

MATERIALS TRANSFER AGREEMENT**Provider:**

U.S. Environmental Protection Agency (EPA)
Office of Research and Development (ORD)
Center for Computational Toxicology and Exposure (CCTE)

Recipient:

The Trustees,

Woods Hole Oceanographic Institution
McMaster University

1a. Provider agrees to transfer to Recipient's Investigator named below the following Research Material:

Chemicals and Materials

- A list identifying selected chemicals from the ToxCast chemical library to be tested by

[Name of Recipient]

- There A copy of the current ToxCast chemical library, or subset, consisting of chemical samples prepared as solution in dimethyl sulfoxide at a concentration of 20 millimolar. Additional chemicals may be provided in the future concurrent with expansion of the ToxCast chemical library.
- Samples of nanomaterials and characterization data on said materials.

Data and Summary Information

- In vitro assay data derived from the ToxCast Program. This data is derived from chemicals analyzed using a variety of high throughput assay techniques. Below this is referred to as the "ToxCast Data".
- There In vivo whole animal toxicology data summary data derived from the EPA Toxicology Reference Database (ToxRefDB). Below this is referred to as the "ToxRefDB Data".
- Summary descriptions of the individual data sets.
- Individual subsets of this data will be delivered to [XXXX] after they have been prepared for use at EPA and cleared for release to

[XXXX]

1b. The Recipient agrees to transfer to the EPA Investigator named below the following Research Material:

- All data or data summaries resulting from chemical screening performed on the ToxCast chemical library.
- Results of any data analyses that include use of provided ToxCast or ToxRef data.
- There Relevant data on these chemicals from non-public sources.
- Unique chemicals for the ToxCast chemical library and subsequent testing by EPA.

2. This Research Material may not be used in human subjects. The Research Material will be used only for research purposes by Recipient's investigator in his/her laboratory, for the research project described below, under suitable containment conditions. This Research Material will not be used for screening, production or sale, for which a commercialization license may be required. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

EPA ONLY: If the data or material that are being transferred constitute human subjects research, please visit the following intranet site to determine if your project needs review and approval by the HSRRO: <https://intranet.ord.epa.gov/human-subject-research/hsr-projects-review>

- There is no Human Subjects material being used in this research.

- Research Plan reviewed and approval by HSRRO:

Name

Date

3. If the data or material that are being transferred involve life sciences research, or more specifically any of the select agents or toxins listed and/or the definitions provided in EPA Order 1000.19 *Policy and Procedures for Managing Dual Use Research of Concern*, then Principal Investigators should consult EPA's Institutional Contact for Dual Use Research of Concern (ICDUR) at DURC@epa.gov before completing the following section. If not, then check the first box below.

- This research does not meet any of the definitions of Dual Use Research of Concern (DURC) and no additional review or oversight are required. The PI must report to the ICDUR any results or changes in the research that meet any of the definitions of DURC.
- This research meets one or more definitions of DURC and requires additional oversight under the *USG Policy for Institutional Oversight of DURC*. The parties to this Agreement are required to comply with EPA Order 1000.19, *Policy and Procedures for Managing Dual Use Research of Concern*.

For information about DURC and EPA Order 1000.19, please visit:

<http://intranet.ord.epa.gov/homeland-security/dual-use-research-concern-durc-policies>

4. This Research Material will be used by Recipient's investigator solely in connection with the following research project ("Research Project") described with specificity as follows:

a. FOA: ADVANCING TOXICOKINETICS FOR EFFICIENT AND ROBUST CHEMICAL EVALUATIONS
EPA-G2019-STAR-D1

b. Grant number: 84002901-0

c. Title: Toxicokinetic screening of zebrafish cytochrome P450 enzymes for in vitro-in vivo extrapolation

d. Lead-PI: Jared Goldstone

Co-PI: Joanna Wilson

e. Lead institution: Woods Hole Oceanographic Institution, Woods Hole, MA 02543

Subcontract institution: McMaster University, Hamilton, Ontario, Canada

f. Project Summary:

Objectives: We propose to determine the metabolic activities of the key xenobiotic cytochrome P450 Phase I enzymes in zebrafish, using novel high-throughput screening methodologies in vitro and in silico, and transgenic knockout animals for in vivo assessments of toxicokinetic parameters in sensitive lifestages. Zebrafish are important test organisms for mechanistic toxicological research and for the safety assessment of manufactured and environmental chemicals, yet aspects of metabolism critical to the use of this model are not fully understood. Furthermore, zebrafish embryos and early ovolarvae provide access to early life stages that are differently sensitive to pollutants, and serve as models for both human and wildlife exposures. Our goal is to develop HTS methods for and determine functionality of cytochrome P450 enzymes that may be most important in pollutant metabolism in zebrafish.

Approach: In vitro screening of heterologously expressed zebrafish CYPs will be performed by analyzing the oxidation of the essential cofactor NADPH to identify putative substrates and uncouplers in the ToxCast Phase 2 library of more than 1800 compounds. We will focus on CYP1A, CYP3A65, CYP3C1, and CYP2Y3, which we believe represent many of the key xenobiotic-metabolizing CYPs in zebrafish. We will determine detailed parent and primary metabolite profiles for top hit compounds, performing more detailed kinetic assays. A novel multiplexed multidimensional GCxGC-MS identification will be used to characterize the metabolite profiles for individual hit compounds. Iterative ligand docking studies will be used to support ligand interactions, to examine how substrates dock into active sites in relation to product profiles, and to predict additional substrates. In vitro-in vivo extrapolation is a key goal in chemical

5. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. Recipient agrees to protect the information claimed as confidential business information from unauthorized disclosure to the extent permitted by law and consistent with EPA's regulations under 40 C.F.R. Part 2, Subpart B. In asserting a claim for protection, the Provider must stamp its Research Material as "CLAIMED AS CONFIDENTIAL BUSINESS INFORMATION." Documents that are stamped with "CLAIMED AS CONFIDENTIAL BUSINESS INFORMATION" represent that the Provider is asserting a confidentiality claim for a period of three (3) years. The foregoing shall not apply to information that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation. Any oral disclosures from Provider to Recipient, which Provider wishes to assert as confidential business information, shall be identified as being confidential business information at the time of the disclosure and by written notice, stamped in the manner stated above, and delivered to Recipient within thirty (30) days after the date of the oral disclosure. Recipient may publish or otherwise publicly disclose the results of the Research Project, but if Provider has given claimed confidential business information to Recipient, such public disclosure may be made only after Provider has had thirty (30) days to review the proposed disclosure to determine if it includes any claimed confidential business information, to the extent such review period is permitted by law.

6. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under his/her direct supervision without advance written approval of Provider. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is completed, the Research Material will be returned to the Provider or disposed, if directed by Provider.

7. This Research Material is provided as a service to the research community. It is being supplied to Recipient with no warranties, express or implied, including any warranty of merchantability or fitness for a particular purpose. Provider makes no representations that the use of the Research Material will not infringe any patent or proprietary rights of third parties.

8. Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. However, if said inventions contain any portion of the Research Material, are derived from the Research Material, or could not have been produced but for the use of the Research Material, Recipient agrees to contact the Provider to determine what ownership interests, if any, the Provider may have, and, where applicable, to negotiate in good faith the terms of a commercial license. Inventorship for a patent application or a commercialized product based on said inventions shall be determined according to United States patent law.

9. When Provider is the EPA: Recipient agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "Government") of the Research Project, the institution, or personnel conducting the Research Project or any resulting product(s). Recipient agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose of the Research Material.

10. When Recipient is the EPA: Provider will not be liable to EPA for any claims or damages arising from EPA's use of the Research Material.

11. The Provider shall have the right to terminate this Agreement at any time if Recipient breaches any of the terms of this Agreement. Upon termination, Recipient shall return to the Provider all unused portions of the Research Materials.

12. Will EPA develop any products or services from information or materials provided by the Recipient?

Yes – go to item A

No – skip to #13 (next clause)

06/02/2021

Item A: The EPA laboratory must coordinate on matters related to Quality Assurance with their QA Specialist.

- If necessary, the Laboratory will develop/has developed a Quality Assurance Plan in coordination with the Quality Assurance Specialist.
- No QA requirements are needed.

13. All notices pertaining to or required by this Agreement shall be in writing and shall be signed by an authorized representative and shall be delivered by hand (including private courier mail service) or sent by certified mail, return receipt requested, with postage prepaid, addressed as follows:

Provider's Contact Information:

Russell Thomas
U.S. EPA Center for Computational Toxicology and Exposure
109 T.W. Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-5776
Thomas.Russell@epa.gov

With a copy to:

Samantha Plishka
U.S. EPA Center for Computational Toxicology and Exposure
109 T.W. Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-2657
Plishka.Samantha@epa.gov

For commercial courier address use:
4930 Old Page Road
Durham, NC 27703

AND

Kathleen Graham
FTTA Program Coordinator
(303) 312-6137
Graham.Kathleen@epa.gov
FTTA@epa.gov

06/02/2021

Recipient's Contact Information:

Gay Yuyitung, Executive Director, McMaster Industry Liaison Office
McMaster Innovation Park
175 Longwood Road South, Suite 305
Hamilton, ON L8P 0A1
905.525.9140 ext. 22649
yuyitun@mcmaster.ca

With a copy to:

Mark Hanson Assistant Director, Grant & Contract Services and Associate General Counsel
Grant & Contract Services, MS#39
266 Woods Hole Road
Woods Hole, MA02543
(508) 289- 2623
mhanson@whoi.edu

14. Paragraphs 2, 5, 7, 8, 9, and 10 shall survive termination.

15. This Agreement shall be construed in accordance with law as applied by the Federal courts in the District of Columbia.

16. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

17. This agreement shall enter into force as of the date of the last signature of the parties and shall remain in effect for one year from said date.

06/02/2021

SIGNATURES

FOR THE RECIPIENT MCMASTER UNIVERSITY

FOR THE RECIPIENT:

Principal Investigator

Principal Investigator





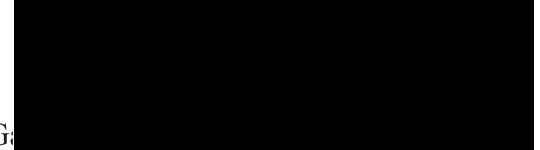
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Joanna Wilson
Professor, McMaster University

Authorized Representative of Institution

Authorized Representative of Institution

Mark E. Hanson Digitally signed by Mark E. Hanson



Mark Hanson
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G.
Executive Director, McMaster Industry
Liaison Office

FOR THE PROVIDER:

Principal Investigator

John Wambaugh
Research Physical Scientist



Authorized Representative of Institution

Russell Thomas, Ph.D.
Director, EPA/ORD/CCTE

