MATERIALS TRANSFER AGREEMENT

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

Recipients:
French Agency for Food, Environmental and Occupational Health & Safety (ANSES), Fougeres Laboratory
and
Research Institute for Environmental and Occupational Health (IRSET/INSERM U1085), 2 Avenue du Pr Léon Bernard, 35043, Rennes, France

1a. Provider agrees to transfer to Recipients' Investigators named below the following Research Material:

Chemicals and Materials

- ☒ A list identifying selected chemicals from the ToxCast chemical library to be tested by Team 1 of IRSET (Dr Olivier Fardel) and ANSES-Fougères (Dr Ludovic Le Hégarat).
- ☐ 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 XXX after they have been prepared for use at EPA and cleared for release to XXXX.

1b. The Recipients agree to transfer to the EPA Investigator named below the following results:

- ☒ All data or data summaries resulting from chemical screening performed on the ToxCast chemical library to Dr. Michael DeVito.
- ☐ Results of any data analyses that include use of provided ToxCast or ToxRef data.

☐ 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: http://intranet.ord.epa.gov/p2/hsr/human-subjects-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 Recipients' investigators solely in connection with the following research project ("Research Project") described with specificity as follows ***(insert description here or use an attachment page if necessary***):

Recipients will attempt to identify pesticide substrates of P-glycoprotein (P-gp) using a MTT assay (i.e., 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay). This cytotoxicity assay will be carried out on an multidrug resistance mutation 1 (MDR1)-overexpressing cell line (MCF7-R; Michigan Cancer Foundation-7 R) in absence/presence of a P-gp inhibitor. If the substance is a P-gp substrate, a differential cytotoxicity will be observed.

Recipients will attempt to identify pesticide inhibitors of P-glycoprotein, and inhibitors and substrates of organic cation transporters (OCTs), organic anion transporters (OATs) or organic anion transporting polypeptides (OATPs) using functional assays based on the use of fluorescent substrates of the transporters. For P-glycoprotein, Recipients will use Rhodamine 123 and Hoechst 33342, which interact with different sites on the pump. For OCTs and OATs/OATPs, Recipient will measure cis-inhibition or trans-stimulation of the reference dyes 4-(4-(dimethylamino)styryl)-N-methylpyridiniumiodide (DiASP) (for OCTs) or fluorescein derivatives (for OATs/OATPs) in transfected Human Embryonic Kidney (HEK)-OCTs, HEK-OATs or HEK-OATPs cells to identify pesticide inhibitors or substrates. Interactions with additional transporters based on fluorescent dye assays will be also be considered.

Recipients will perform the tests on its high-content screening platform.

5. Recipients may publish or otherwise publicly disclose the results of the Research Project, In all oral presentations or written publications concerning the Research Project, Recipients will acknowledge Provider's contribution of this Research Material unless requested otherwise.

6. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipients' investigators therefore agree to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under their 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 Recipients 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. Recipients 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, Recipients agree 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: Recipients agree 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). Recipients agree to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses, and losses arising out of Recipients' 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 any of the Recipients breach any of the terms of this Agreement. Upon termination, all Recipients 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)

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

Michael DeVito, Ph.D.
U.S. EPA Center for Computational Toxicology and Exposure
109 T.W. Alexander (MC-E205-C)
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With a copy to:
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For commercial courier address use:
4930 Old Page Road
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AND

Kathleen Graham
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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 Recipients 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.

SIGNATURES

FOR THE RECIPIENTS:

Principal Investigators

[redacted] [redacted]

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Authorized Representatives of Institution

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Michel SAMSON Date
Dr, Director of IRSET
Michel.samson@univ-rennes1.fr

FOR THE PROVIDER:

Principal Investigator

[redacted] [redacted]

Michael DeVito, Ph.D. Date
Director, EPA/ORD/CCTE/CCED
Devito.Michael@epa.gov

Authorized Representative of Institution

[redacted] [redacted]

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