MATERIALS TRANSFER AGREEMENT

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

Recipient:
Health Canada (HC)
Healthy Environments and Consumer Safety Branch (HECSB)
Environmental Health Science and Research Bureau (EHSRB)

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

Chemicals and Materials

- ☒ A copy of select per- and poly-fluoroalkylated substances (PFAS) from the current ToxCast chemical library consisting of chemical samples prepared as solution in dimethyl sulfoxide at a concentration of 30 millimolar (maybe modified dependent upon specific chemical properties). 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".
- ☒ 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.

Recipient agrees to transfer to the EPA Investigator named below:

- ☒ All data resulting from chemical screening performed on the ToxCast chemical library.
- ☐ Relevant data on these chemicals from non-public sources.
- ☐ Unique chemicals for the ToxCast chemical library and subsequent testing.

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.

x 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.

x 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. Does the Research Material include specimens or data derived or collected from human subjects?
___x__ Yes – Go to item #4(a).
__ ___ No – Skip to item #5.

4(a). Does the Research Material include specimens or data derived or collected from

fetuses, children, pregnant women, or nursing women?
_____ Yes
__x__ No

4(b). Was the Research Material obtained under a protocol that was reviewed and approved by an Institutional Review Board (IRB) that operated in accordance with the requirements of EPA Regulation 40 CFR 26, HHS Regulation 45 CFR 46, or any other Federal Regulation for the protection of human research subjects?
__x__ Yes (Please indicate the applicable Regulation here
_____ and provide copies of the protocol and IRB approval documents.)

All human organs/tissues are sourced by ***InSphero's supplier*** within the U.S. through non-profit Human Tissue and Organ Recovery and Placement Networks (HTORPN) that procure tissues via Organ Procurement Organizations (OPO) that are certified by the Centers for Medicare and Medicaid services (CMS) and abide by CMS regulations. ***InSphero's and their supplier*** are not part of this research effort and only represent the source to purchase tissues for *in vitro* assays. By federal law, all OPOs must be members of the Organ Procurement and Transplantation Network (OPTN) and, as such, are members of the United Network for Organ Sharing (UNOS) which is a privately-operated entity that has a contract with the U.S. government to operate the (OPTN).

These OPOs operate under a set of standards established by the Association of Organ Procurement Organizations (AOPO) and the United Network of Organ Sharing (UNOS). Each OPO operates individually under its own protocol, and these standard operating procedures must conform to each respective state's Uniform Anatomical Gift Act (UAGA) as well as the hospitals' policies in each region. All OPOs are members of UNOS and agree to comply with all applicable provisions of the National Organ Transplant Act (NOTA), as amended, 42 U.S.C. 213 et seq.; OPTN Final Rule, 42 CFR Part 121.

Consent for research is obtained by each individual OPO that procures human organs/tissue in compliance with local, state, and federal guidelines including the UAGA. Each consent form includes language that indicates that the donated tissue can be used for research and is an anatomical gift for which no compensation is given. OPO maintain the informed consent records from each donor, and it is the policy of each HTORPN to confirm the existence of informed consent for research purposes prior to transport of organs to ***InSphero's supplier***. This procedure is intended to ensure that ***InSphero's supplier*** manufactures human-derived products only when informed consent has been granted for research use of those specific organs.

_____ No (Please provide explanation with documentary support as appropriate.)

4(c). Can the Provider of the Research Material identify the subjects directly or through identifiers (codes) linked to the subjects?
_____ Yes – The Recipient's use of the Research Material may be human subject's research subject to 40 CFR 26. Go to item #3(d).
__x__ No – The Recipient's use of the Research Material is not human subjects research subject to 40 CFR 26. Skip to item #4.

4(d). Is the Provider of the Research Material prohibited by this agreement from releasing information to the Recipient that might allow the identification of any of the subjects, including but not limited to the key to any existing code?
_____ Yes – The Recipient's use of the Research Material is not human subjects research subject to 40 CFR 26. Skip to item #4.
_____ No – The Recipient's use of the Research Material may be human subjects research subject to 40 CFR 26. Go to item #3(e).

4(e). Is the Research Material publicly available?
_____ Yes – The Recipient's use of the Research Material is human subjects research that is exempt from 40 CFR 26.
_____ No – The Recipient's use of the Research Material is human subjects research that may be subject to 40 CFR 26 and must be further evaluated accordingly by the EPA Human Subjects Review Official.

5. 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:

Per- and poly-fluoroalkylated substances (PFAS) are a large class of man-made chemicals that are ubiquitously found in the environment due to their wide variety of industrial and commercial uses, their persistence and their high mobility. There are concerns for exposure through drinking water and potential adverse health effects including liver and kidney toxicity, increased cholesterol levels and delays in mammary gland development that may occur at low levels of exposure to PFAS. Although there is a growing body of knowledge on PFOS (perfluorooctanesulfonic acid) and PFOA (perfluorooctanoic acid) toxicity, there is little known about the many other PFAS (i.e., considered 'data-poor'). As such, Health Canada has identified toxicity testing for PFAS as a research priority.

The research on the PFAS provided by the EPA will employ gene expression profiling in primary human hepatocytes in an effort to facilitate read-across for various data-poor PFAS. The research is a case study under the umbrella of the Accelerating the Pace of Chemical Risk Assessments (jointly lead by the US Environmental Protection Agency, US National Toxicology Program, European Food Safety Authority, and European Chemicals Agency) and will demonstrate the use of gene expression profiling for chemical risk assessment while providing valuable information on priority PFAS.

6. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. To the extent permitted by law, Recipient agrees to treat as confidential, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL" for a period of three (3) years from the date of its disclosure to recipient. 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 the Provider wishes to be treated as confidential shall be identified as being Confidential at the time of the disclosure and by written notice 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 Confidential 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 Confidential information, to the extent such review period is permitted by law.

7. 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.

8. 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.

9. 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.

10. 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.

11. 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.

12. 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.

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

_____ Yes – go to item A

__x__ No – skip to #14 (next clause)

Item A: The EPA has a long history of applying principles of quality assurance/quality control to all technical work conducted by or for the Agency (CIO 2106: USEPA Quality Policy). Given EPA is receiving metabolomics and screening data and will use the metabolomics and screening data for Agency purposes, the Recipient is required to provide EPA with documentation such as a quality manual, describing their organization's quality system. In lieu of such documentation, Standard Operating Protocols for compound handling and the assays performed are acceptable or documentation showing third party accreditation to a relevant standard and scope is also acceptable for documenting an organization's quality system. EPA requirements for quality management plans can be found at this URL:
http://www.epa.gov/quality/qa_docs.html

14. 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 National Center for Computational Toxicology (NCCT)
109 T.W. Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-5776
thomas.russell@epa.gov

Provider's Administrative Contact Information:

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US EPA
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For commercial courier address use:
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AND

Kathleen Graham
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Recipient's Contact Information:

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Any false or misleading statements made, presented, or submitted to the Government, including any material omissions, under this Agreement and during the course of negotiation of this Agreement are subject to all applicable civil and criminal statutes including 31 U.S.C. ' ' 3801-3812 (civil liability), 18 U.S.C. ' 1001 (criminal liability), and 31 U.S.C. ' ' 3729-33 (False Claims Act).