MATERIALS TRANSFER AGREEMENT

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

Recipient:
Simulations Plus, Inc.
42505 10th Street West
Lancaster, CA 93534

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

Chemicals and Materials

X A list identifying selected chemicals from the DSStox chemical library to be simulated by Simulations Plus.

Data and Summary Information

X Measured and predicted physico-chemical properties informing toxicokinetics behavior
X Initially, meta-data describing a series of *in vivo* toxicokinetic experiments collected with an NCCT database of chemical concentration vs. time data curated from EPA and open literature experiments
X Subsequently, the actual concentration data from the NCCT database

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

X *In silico* predictions of toxicokinetic summary statistics such as volume of distribution, peak (maximum) serum concentration, area under the plasma concentration vs. time curve.

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.

3. 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

Does the research involve specimens or data derived or collected from human subjects?

[x] No
[ ] Yes – I am seeking review and approval from the HSSRO. Assurance Number____

4. The Dual Use Research of Concern (DURC) Internal Review Entity (IRE) has determined that:

[x] this research does not meet the DURC definition and no additional review and oversight are required. The PI must report to the IRE any results or changes in the research such that one or more of the 7 categories of experimental effects may apply, or if the PI feels that the research may be DURC.

□ this research meets the DURC definition and requires additional oversight under the *USG Policy for Institutional Oversight of DURC*. Corresponding USG funding agency will be notified and a draft of the mitigation plan will be submitted within 90 days of this determination.

□ Mitigation Plan submitted to the funding agency on

□ Approved mitigation Plan on file

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

To improve the state of predictive toxicokinetic (TK) modeling, NCCT will share with Simulations Plus the data from NCCT's TK Concentration vs. Time database (TKCvT). Simulation Plus agrees to share their concentration vs time predictions and will consult with EPA to assist in the analyzation of those predictions. Simulations Plus requests NCCT provide a set of TK experimental conditions including chemical, route of administration, dose protocol, species, and (when available, strain, sex, and life-stage). Using these conditions, Simulations Plus will predict concentration vs. time data for the experiment. Once predictions are made, Simulation Plus will share these data with NCCT, and then literature extracted concentration vs. time data from the NCCT TKCvT database will be provided to Simulations Plus.

By comparing results of the predictive PK algorithms to the NCCT TKCvT database we aim to identify the strengths and limitations of *in silico* tools for predicting TK, and refine tools developed by both Simulations Plus and NCCT.

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 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:
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With a copy to:
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AND

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With a copy to:
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