MATERIALS TRANSFER AGREEMENT

Provider:

U.S. Environmental Protection Agency, National Center for Computational Toxicology

Recipient:

WatchFrog S.A.

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

A. A copy of all or some of the ToxCast™ chemical library consisting of 50 microliters each of 320 chemical samples prepared as solutions in dimethyl sulfoxide at a concentraton of 20 millimolar.
B. As an alternative to (A), EPA and Watchfrog will identify 15 compounds with a range of apparent thyrotoxicity, based upon ToxCast in vitro and in vivo data. WatchFrog will acquire 0.5g samples of each of the 15 compounds selected. If Watchfrog is not able to efficiently acquire any compounds, EPA will attempt to supply them, and organize a shipment to WatchFrog's premises at EPA's cost. Identification of each sample (chemical name and CAS number) will be provided to WatchFrog.
C. In vitro assay data derived from Phase I of the ToxCast™ Program. This data is derived from a set of 320 chemicals which were analyzed using a variety of assay techniques. Below, this is referred to as the "ToxCast™ Data".
D. In vivo whole animal toxicology summary data derived from Office of Pesticide programs (OPP) Data Evaluation Records (DERs) and compiled in the EPA Toxicology Reference Database (ToxRefDB). This data is derived from a subset of the 320 ToxCast™ Phase I chemicals. Below, this is referred to as the "ToxRefDB Data".

E. Summary descriptions of the individual data sets.
F. Individual subsets of this data will be delivered to the recipient after they have been prepared for use at the EPA and cleared for release to the Recipient.

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. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

2(a). Were Research Materials collected according to 45 C.F.R. Part 46, "Protection of Human Subjects?"

___ Yes (Please provide Assurance Number:_____)

___ No

_X_ Not Applicable (Materials not collected from humans)

3. This Research Material will be used by Recipient's investigator solely in connection with the following research projects described with specificity as follows *(use an attachment page if necessary)*:

The objectives of the study:

A. Predictive evaluation using WatchFrog's thyroid test of 15 compounds selected by EPA in the perspective of OECD recommended thyroid test on amphibian metamorphosis.

B. Comparative analysis of in vivo results using WatchFrog with other data generated in the EPA's ToxCast program

The Research Study consists of the following activities to be conducted by WatchFrog on up to 15 selected compounds:
Xenopus laevis embryos bearing a thyroid responsive construct derived from TH-bZip promoter upstream of fluorescent protein coding sequence will be exposed to 15 different compounds. Using this in vivo model, WatchFrog will perform physiological-based screen for potential thyroid signalling disruptors. Experiments will be performed using stage 45 to 47 tadpoles (stages determined according to Nieuwkoop and Faber). The care and treatment of animals used in this study will be performed in accordance with institutional and national guidelines (EU regulation Dir 86/609/EEC). Each compound will be tested on a minimum of 20 embryos. Each compound will be tested at three different concentrations. Tests will be performed in defined media (American Society for Testing and Materials FETAX Guideline 1991, 1999). Each test will be performed in presence (and absence) of 5.10-9M of thyroid hormone (T3) to detect both pro and anti-thyroid effects. Two different groups of control will be added in each experiment, a group receiving no T3 and a group receiving only T3. Renewal of test sample will be done each day during the test. Fluorescence measurement will be performed at the end of test after 72 hours of treatment. Fluorescence reading will be performed putting test-embryos into 96 well plates. Before reading fluorescence embryos will be washed in FETAX media and anesthetized. Statistical treatment of results will be performed following OECD guidelines. Each test (at each concentration) will be performed three times.

4. 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 five (5) 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, except when the shortened time period is pursuant to a court order or to the extent such review period is permitted by law. No results of the Research Project will be disclosed to third parties without the prior agreement from both parties.

5. The Recipient will provide to the Provider all testing results obtained by the Recipient using the Research Material. Recipient acknowledges that the Provider will make such testing results freely available to the public, once the results have been published in a peer-reviewed journal article. The goal of both parties is to publish the data and co-author a peer-reviewed journal article describing the results. All publications will require the prior agreement from both parties.

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. This Agreement shall begin on the date of its execution and continue for twelve (12) months thereafter, and shall automatically renew for successive year long periods (a)

unless one party notifies the other party no sooner that thirty (30) days prior to such renewal date that it elects not to renew the Agreement, or (b) unless earlier terminated as provided in the next sentence. 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. 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 Official and Mailing Address:
Robert J. Kavlock, Director
National Center for Computational Toxicology (NCCT)
US EPA (MD-205-01)
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Recipient's Official and Mailing Address:
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