MATERIALS TRANSFER AGREEMENT

EPA:

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

GSK:

SmithKline Beecham Corporation doing business as GlaxoSmithKline, having a place of business at Five Moore Drive, Research Triangle Park, North Carolina 27709 ("GSK") and its Affiliates.

WHEREAS, the EPA wishes to obtain GSK Compounds to use in certain test assay panels, and whereas GSK wishes to have GSK Compounds evaluated on such test panels, the parties agree as follows:

"Affiliate" means any corporation, firm, partnership or other entity which directly or indirectly controls, is controlled by, or is under common control (50% or more ownership) with either of the parties.

1. EPA agrees to receive GSK's compounds, in any form or any of its intermediates and derivatives ("GSK Compound"), in order to perform the research activities, further described in Exhibit A, and known as the "ToxCast™ Program.

2. The GSK Compounds:

   a. are the property of GSK and all existing rights, including without limitation, patent rights in or to the GSK Compounds, and will remain the property of GSK.

   b. will be used with caution and for research purposes only, and shall not be used for research involving human subjects.

   c. will be used only by the EPA in the ToxCast™ Program described below, under suitable containment conditions.

   d. will not be used for screening, production or sale, for which a commercialization license may be required.

Both GSK and EPA agree to comply with all applicable laws, rules, guidelines and regulations applicable to the use, storage, shipping and the handling of the GSK Compounds and ToxCast™ Program.

3. Do the GSK Compounds and/or associated pre-clinical/clinical data being transferred ("Testing Results") include specimens or data derived or collected from human subjects?

__X__ Yes – Go to item #3(a).
__ __ No – Skip to item #4.

3(a). Do the Testing Results include specimens or data derived or collected from fetuses, children, pregnant women, or nursing women?

_____ Yes
X_____No

3(b). Were the Testing Results obtained under a protocol that was 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
_____ No (Please provide explanation with documentary support as appropriate.)

3(c). Can the Provider of the Testing Results identify the subject directly or through identifiers (codes) linked to the subjects?

_____ Yes – Go to item #3(d)
X_____ No – Skip to Item #4.

3(d). Is the Provider of the Testing Results 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 – Skip to item #4
_____ No – Go to item #3(e).

3(e). Are the Testing Results publicly available?

_____ Yes
_____ No.

4. The GSK Compounds will be used by the EPA solely in the ToxCast™ Program described in Exhibit A of this Agreement.

5. In all oral presentations or written publications concerning the ToxCast™ Program, EPA will acknowledge GSK's contribution of the GSK Compounds unless requested otherwise by GSK. To the extent permitted by law, EPA agrees to treat as confidential, any of GSK's written information about the GSK Compounds that is stamped "CONFIDENTIAL". The foregoing shall not apply to information that is or becomes publicly available through no fault of EPA or which is disclosed to EPA without a confidentiality obligation. The parties acknowledge that GSK will transfer to EPA preclinical and clinical data relating to the kinetics and toxicity of the GSK Compounds. These data shall be considered non-confidential unless indicated by GSK as such per this Section 5. Any oral disclosures from GSK to EPA which GSK wishes to be treated

as confidential shall be identified as being Confidential at the time of disclosure and by written notice delivered to EPA within thirty (30) days after the date of the oral disclosure. EPA may publish or otherwise publicly disclose the results of the ToxCast™ Program, but if GSK has given Confidential information to EPA, such public disclosure may be made only after GSK has had sixty (60) days to review and comment on the proposed disclosure to determine if it includes any Confidential information to the extent such review period is permitted by law.

6. The EPA will provide to GSK in writing all results and conclusions of any research obtained by the EPA utilizing the GSK Compounds in the ToxCast™ Program, and EPA will not use those results and conclusions to file any patent applications that claim the manufacture, use or sale of the GSK Compounds.

Both parties grant to each other a non-exclusive license to use the results of the ToxCast™ Program using the GSK Compounds in their own research only.

7. The GSK Compounds represent a significant investment on the part of GSK and are considered proprietary to GSK. The EPA therefore agrees to retain control over the GSK Compounds and further agrees not to transfer the GSK Compounds to other people or parties without advance written approval of GSK. GSK reserves the right to distribute the GSK Compounds to others and to use it for its own purposes.

8. Both the ToxCast™ Program and the GSK Compounds are provided as a service to the research community. They are being supplied "as is" with no representations, warranties, express or implied, of any kind, including any warranty of merchantability or fitness for a particular purpose. Neither party makes any representations that the use of the ToxCast™ Program or GSK Compounds will not infringe any patent or proprietary rights of third parties.

9. EPA shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the performance of the ToxCast™ Program. However, notwithstanding Section 6 above, if said inventions contain any portion of the GSK Compounds, are derived from the GSK Compounds, or could not have been produced but for the use of the GSK Compounds, the EPA agrees to contact GSK to determine what ownership interests, if any, GSK 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. Neither this Agreement nor the performance of it by EPA will transfer to EPA any proprietary right, title, interest or claim in or to any of the GSK Compounds (including any intellectual property rights subsisting therein).

10. GSK agrees not to claim, infer or imply endorsement by the Government of the United States of America (hereinafter deferred to a "Government") of the ToxCast™ Program, the institution or personnel conducting the ToxCast™ Program or any resulting product(s).

11. Either party shall have the right to terminate this Agreement at any time. Upon termination, the performance of the ToxCast™ Program using the GSK Compounds shall end, and the EPA shall return to GSK all unused portions of the GSK Compounds

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:

EPA's Official and Mailing Address:

Robert J. Kavlock, Director
US EPA/ORD/NCCT
109 TW Alexander Dr., MD-B-205-01
Research Triangle Park, NC 27711

GSK's Official and Mailing Address:

Patrick J. Wier
Vice President Safety Assessment
GlaxoSmithKline
709 Swedeland Road
P. O. Box 1539
King of Prussia, PA 19406-0939

Phone: 610 270 7604
FAX: 610-270-7504
EMAIL: Patrick.J.Wier@gsk.com

or

Neal Cariello
GlaxoSmithKline
Five Moore Drive
Building 9, Room 2011
Research Triangle Park, NC 27709

Phone: 919 483 6782
FAX: 919 483 0131
EMAIL: Neal.F.Cariello@gsk.com

13. Paragraphs 8, 9, 10 and 11 shall survive termination.

GSK – USA EPA Collaboration on ToxCast

Introduction

The U.S. Environmental Protection Agency (EPA) is developing methods for utilizing computational chemistry, high-throughput screening (HTS), and various toxicogenomic technologies to predict potential for toxicity and prioritize limited testing resources toward chemicals that likely represent the greatest hazard to human health and the environment. This chemical prioritization research program, entitled "ToxCast" is being initiated with the purpose of developing the ability to forecast toxicity based on bioactivity profiling. The proof-of-concept phase of ToxCast will focus upon chemicals with an existing, rich toxicological database in order to provide an interpretive context for the ToxCast data. This set of several hundred reference chemicals will represent numerous structural classes and phenotypic outcomes, including tumorigens, developmental and reproductive toxicants, neurotoxicants, and immunotoxicants. The ToxCast program will evaluate chemical properties and bioactivity profiles across a broad spectrum of data domains: physical-chemical, predicted biological activities based on existing structure-activity models, biochemical properties based on HTS assays, cell-based phenotypic assays, and genomic and metabolomic analyses of cells. These data will be generated through a series of external contracts, along with collaborations across EPA, with the National Toxicology Program, and with the National Institutes of Health Chemical Genomics Center. The resulting multidimensional data set provides an informatics challenge requiring appropriate computational methods for integrating various chemical, biological and toxicological data into profiles and models predicting toxicity.

Objectives

There are multiple objectives to this collaboration:

1) To put predictive assay profiles for pesticides into context by comparing them to profiles of compounds that have known human or animal effects
2) Identify predictive assays or profiles that may help in the rapid screening out of compounds likely to fail for safety reasons in animal toxicity testing or clinical trials
3) Evaluate new technology platforms for their applicability to the drug discovery and development process
4) Identify and evaluate new computational approaches that will allow GSK to extract greater value from the data it generates on novel candidates

Work Plan

The collaboration will consist of GSK providing the EPA with chemical matter for proprietary compounds that have been discontinued from further development. GSK will also supply the chemical structures and in vivo study data on the toxicity of these compounds both in pre-clinical species and/or humans. No information on the primary pharmacology or the intended therapeutic indication will be disclosed.

The EPA in collaboration with its partners, will then profile the compounds in the in vitro assay panels at no additional cost to GSK. Data from these experiments will be made available to GSK on completion of the experiments and in advance of being made available in the public domain.

GSK will also provide the EPA with clinical chemistry and histopathological information regarding non-proprietary model hepatotoxicants which GSK has tested.

Exhibit A: Brief Description of the Assays

Contractor	Assay Type	Number of assays or endpoints	ToxCast Assays Endpoint References	Comments
ACEA Biosciences, Inc.	real-time cell electronic sensing	1	Xing et al 2006. Microelectronic cell sensor assay for detection of cytotoxicity. Toxicol In Vitro assay for detection of cytotoxicity and prediction of acute toxicity. Toxicol in Vitro 20:995-1004; www.aceabio.com	cell-based assy; impedance measurement of cells; general proliferation/toxicity readout
Attagene, Inc.	transcription factor activities; reporter gene expression	67	US Patent Application 20060160108; populations of reporter sequences and methods of their use; www.attagene.com	HepG2-based reporter assay system; 43 transcription facto and 24 nuclear hormone receptors; 25 uM conc
BioSeek, Inc.	complex primary human cell-based	87	Berg et al 2006. Characterization of compound mechanisms and secondary activities by BioMAP analysis. J Pharmacol Toxicol Methods 53:67-74; www.bioseekinc.com	Variety of primary human cel types; bronchial, epithelial, dermal fibroblasts, keratinocytes, HUVEC; 4 con measures protein readouts; results compared to Bioseek's database/reference compound
Cellumen, Inc.	cellular high content screening (HCS)	11	Giuliano et al 2006. Sytems cell biology based on high-content screening. Methods Enzymol 414:601-19; www.cellumen.com	HepG2 cell line; 10 conc, 3 timepoints. 11 endpoints of stress, mito, DNA, cytoskeletal, nuclear readouts
Compound Focus, Inc. / BioFocus DPI Expression Analysis, Inc.	chemical procurement and handling; in vitro genomics; gene expression	>20K	www.sbsonline.org/publications/news /issues/2005/index.php; www.biofocus.com. Shi et al 2008. The Microarray Quality Control (MAQC) project shows inter- and intraplatform reproducibility of gene expression measurements. Nat Biotechnol 2006 Sep 24(9) 1151-61	DNA microarray with rat or mouse primary hepatocytes; 1 conc of compound

In Vitro ADMET Laboratories (IVAL), LLC.	cell culture and co-culture	1	Li AP 2007. Human hepatocytes: isolation, cryopreservation and applications in drug development. Chem Biol Interact 168:16-29. www invitroadment.com	Rat of mouse primary hepatocytes, co-cultured with metabolically incompetent cells line; looks for metabolic activation; 4 conc
NovaScreen Biosciences Corp.	biochemical and cellular high throughput screening (HTS)	240	www.novascreen.com	Bioprint/CEREP in vitro assays including P450 enzymes (10 uM), enzymes ic channels and receptors (25 uM)
Phylonix Pharmaceuticals	zebrafish developmental toxicity	13	Parng et al 2007. Neurotoxicity assessment using zebrafish. J Pharmacol Toxicol Methods 55:103-112. www.phylonix.com	Developmental assessment as in DSRD; 1 conc tested
NIH Chemical Genomics Center	biochemical and cellular high throughput screening (HTS)	>10	Inglese et al. Quantitative high throughput screening; a titration-based approach that efficiently identifies biological activities in large chemical libraries. Proc Natl Acad Sci USA 103:11473-8; www.ncgc.nih.gov	10 conc; nuclear receptor transactivation assays; overla with Attagene assays