MATERIALS TRANSFER AGREEMENT

EPA:

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

Pfizer:
Pfizer Inc, having a principal place of business at 235 East 42nd Street, New York, ("Pfizer") New York, 10017 and its Affiliates

WHEREAS the EPA wishes to obtain Pfizer Compounds to use in certain test assay panels, and whereas Pfizer wishes to have Pfizer 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 with either of the parties.

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

2. The Pfizer Compounds:
   a. are the property of Pfizer and all existing rights including, without limitation, patent rights in or to the Pfizer Compounds will remain the property of the Pfizer.
   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 Pfizer and EPA agree to comply with all applicable laws, rules, guidelines and regulations applicable to the use, storage, shipping and the handling of the Pfizer Compounds and ToxCast™ Program.

3. Do the Pfizer Compounds and/or associated pre-clinical/clinical data being transferred ("Testing Results") include specimens or data derived or collected from human subjects?
_XX_ 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
__XX_ 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?
_XX_ Yes
_____ No (Please provide explanation with documentary support as appropriate.)

3(c). Can the Provider of the Testing Results identify the subjects directly or through identifiers (codes) linked to the subjects?
_____ Yes – Go to item #3(d).
_XX__ 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 Pfizer 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 Pfizer's contribution of the Pfizer Compounds unless requested otherwise by Pfizer. To the extent permitted by law, EPA agrees to treat as confidential, any of Pfizer's written information about the Pfizer Compounds that is stamped "CONFIDENTIAL." The foregoing shall not apply to information that is or becomes publicly available or which is disclosed to EPA without a confidentiality obligation. The parties acknowledge that Pfizer will transfer to EPA preclinical and clinical data relating to the kinetics and toxicity of the Pfizer Compounds. These data shall be considered non-confidential unless indicated by Pfizer as such per this Section 5. Any oral disclosures from Pfizer to EPA which Pfizer wishes to be treated as confidential shall be identified as being Confidential at the time of the 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 Pfizer has given Confidential information to EPA, such public disclosure may be made only after Pfizer 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 Pfizer in writing all results and conclusions of any research obtained by the EPA utilizing the Pfizer 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 Pfizer Compounds.

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

Both parties acknowledge that such testing results shall be made freely available to the public following the review process described in section 5 above.

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

8. Both the ToxCast™ Program and the Pfizer 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 Pfizer 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 Pfizer Compounds, are derived from the Pfizer Compounds, or could not have been produced but for the use of the Pfizer Compounds, the EPA agrees to contact Pfizer to determine what ownership interests, if any, Pfizer 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 letter 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 Pfizer Compounds (including any intellectual property rights subsisting therein).

10. Pfizer agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "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 Pfizer Compounds shall end, and the EPA shall return to Pfizer all unused portions of the Pfizer 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

Pfizer's Official and Mailing Address:

Pfizer Global Research & Development
50 Pequot Avenue
New London, CT 06320
Attn.: President, PGRD,
with copy to: General Counsel PGRD
and Lawrence M. Zaccaro
phone: 860-441-1853
fax: 860-715-7880
email: lawrence.m.zaccaro@pfizer.com

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

14. This Agreement shall be construed in accordance with law as applied by the Federal courts in the District of Columbia.

15. The undersigned, EPA and Pfizer, expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

16. Neither party is obligated to negotiate or enter into any other agreement, and any evaluation or discussions may be terminated at the sole discretion of either party at any time and for any reason. Unless and until a definitive agreement is executed and delivered by the parties, neither party is under any legal obligation of any kind with respect to any transaction, except for the matters specifically agreed to in this letter agreement.

17. A waiver by either party of any term or condition of this letter agreement must be in writing signed by the waiving party. A waiver in one instance of a term or condition shall not be deemed a waiver of such term or condition in any other instance.

18. This letter agreement sets forth the parties' entire understanding about its subject matter and supersedes any other agreement or understanding between the parties about its subject matter. Neither party can assign, amend, or terminate any part of this letter agreement except in writing signed by both parties.

19. This letter agreement may be executed in two or more counterparts (including by facsimile), each of which shall be deemed an original, and all of which together shall constitute one and the same instrument.

Pfizer – US 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 effects
2) Identify predictive assays or profiles that may help in the rapid screening out of compounds likely to fail for safety reasons in 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 Pfizer to extract greater value from the data it generates on novel candidates

Work Plan

The collaboration will consist of Pfizer providing the EPA with chemical matter for approximately 100 proprietary compounds that have been discontinued from further development due to safety reasons. Pfizer will also supply the chemical structures and in vivo study data on the toxicity of these compounds both in pre-clinical species and human. 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 Pfizer. Data from these experiments will be made available to Pfizer on completion of the experiments and in advance of being made available in the public domain.

Brief Description of the Assays

Contractor	Assay Type	# 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 and prediction of acute toxicity. Toxicol In Vitro assay for detection of cytotoxicity and prediction of acute toxicity. Toxicol In Vitro20:995-1004; www.aceabio.com	cell-based assay; 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 factors and 24 nuclear hormone receptors; 25 uM conc
BioSeek Inc.	complex primary human cellbased	87	Berg et al 2006. Characterization of compound mechanisms and secondary activities by BioMAP analysis. J Pharmacol Toxicol Methods 53:67-74;bioseekinc.com	Variety of primary human cell types: bronchial epithelial, dermal fibroblasts, keratinocytes, HUVEC; 4 conc: measures protein readouts; results compared to Bioseek's database/reference cmpds
Cellumen, Inc.	cellular high content screening (HCS)	11	Giuliano et atl 2006. Systems 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 readounts
Compound Focus, Inc. /	chemical procurement and	n/a	www.sbsonline.org/publications/news/issues/	

BioFocus DPI	handling		2005_12/index.php ; www.biofocus.com	
Expression Analysis, Inc.	in vitro genomics; gene expression	>20K	Shi et al 2006. The MicroArray Quality Control (MAQC) project shows inter- and intraplatform reproducibility of gene expression measurements. Nat Biotechnol 2006 Sep;24(9):1151-61; www.expressionanalysis.com.	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.invitroadmet.com	Rat or mouse primary hepatocytes, co-cultured with metabolically incompetent cell line; looks for metabolic activation; 4 conc
NovaScreen Biosciences Corp	biochemical and cellular high throughput screeening (HTS)	240	www.novascreen.com	Bioprint/CEREP in vitro assays including P450 enzymes (10 uM), enzymes ion 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 screeening (HTS)	>10	Inglese et al 2006. Quantitative highthroughput screening: a titration-basedapproach 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 trans-activation assays; overlap with Attagene assays