521-09

MATERIALS TRANSFER AGREEMENT

Provider:

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

Recipient:

Salman R. Khetani, PhD
Director of Research
Hepregen Corporation
200 Boston Avenue, Suite 1100
Medford, MA 02155
Phone (cell): 617-646-9503
Email: srkhetani@gmail.com; skhetani@mit.edu

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

A. A copy 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. 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".
C. 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".
D. Summary descriptions of the individual data sets.
E. 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) See attached email

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)*:

For this project, we will use the micropatterned coculture 96-well plates created using primary rat or human hepatocytes (described in Khetani, S.R. and Bhatia, S.N. Microscale culture of human liver cells for drug development. Nature Biotechnology, 26 (1): 120-126). Rat hepatocytes will be isolated in Hepregen's laboratory using existing protocols, while primary human hepatocytes will be purchased from registered hepatocyte vendors (CellzDirect, BD-Gentest, Celsis In vitro technologies). Rat micropatterned cocultures will be exposed to reference compounds for 24-48 hours, RNA will be collected and sent to the EPA (the "RNA Data") for analysis on Illumina whole genome expression arrays. Data acquired by the EPA will be shared with Hepregen to design further experiments using the rat micropatterned coculture platform. Provider shall not publicly disclose the RNA Data without prior written approval of Recipient. Human micropatterned cocultures in 96-well plates will be exposed to one or more concentrations of the 320 EPA ToxCast™ compounds, and after 24-48 hours of incubation, RNA will be extracted and expression levels of ~100 drug metabolism genes (agreed upon by the EPA and Hepregen) will be evaluated using the Luminex xMAP technology accessible at the Broad Institute of MIT and Harvard, or some other technology. Data will be shared with the EPA for their predictive modeling.

4. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material, if used, 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 through no fault of the Recipient; was independently developed or discovered by the Recipient without use of the Confidential Information; is disclosed without restriction to the Recipient in good faith by a third party who is in lawful possession thereof and who has the right to make such disclosure; or is required to be disclosed as required by applicable laws or by order or a court or governmental agency. If Recipient is required by judicial or administrative process to disclose Confidential Information, the Recipient shall promptly notify the Provider and shall allow the Disclosing Party a reasonable time to oppose such process. Recipient shall only disclose such Confidential Information required by an appropriate order, and shall preserve the

confidentiality of all such Confidential Information that is not necessary to be disclosed unless otherwise required by judicial or administrative process.. 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.

5. The Recipient will provide to the Provider all testing results obtained by the Recipient using the Research Material. Provider acknowledges that Recipient owns all testing results and Recipient acknowledges that the Provider will make such testing results freely available to the public upon review and approval by the Recipient.

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 against all liabilities, demands, damages, expenses and losses arising out of Recipient's use of the Research Material in the Research Project.

10. When Recipient is the EPA (including for the purpose of the EPA's receipt and analysis of RNA samples and RNA Data in accordance with Section 3): 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 upon written request of the Provider. Recipient may retain one copy of the Confidential Information solely for the purpose of monitoring its obligations under this Agreement.

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)
4930 Old Page Rd.
Research Triangle Park, NC 27711

Recipient's Official and Mailing Address:
Salman R. Khetani, Director of Research
Hepregen Corporation
200 Boston Avenue, Suite 1100
Medford, MA 02155

Phone (cell): 617-646-9503

Re: EPA ToxCast-Hepregen MTA--Additional Questions

Salman Khetani to: Karen Dean 02/02/2009 10:55 AM
Cc: Bonnie Fendrock, David Dix, Keith Houck

History: This message has been replied to.

Karen,

Please note my new email address: skhetani@hepregen.com.

Regarding your questions, we plan to use human liver cells which we purchase from vendors permitted to sell products derived from human organs procured in the U.S. by federally designated Organ Procurement Organizations. These vendors include: CellzDirect/Invitrogen, Lonza, Becton Dickinson, Celsis In Vitro Technologies and ADMET Technologies. We are not provided the donor's identity. We just get the isolated cells.

So, I am not sure if question 7 and its sub-components applies to us since I believe it is for live human subjects that we come into contact directly, correct? Please let me know if this is not the case.

Regards,
Salman

Salman R. Khetani, PhD
Director of Research
Hepregen Corporation

200 Boston Ave
Medford, MA 02155
Phone: 781-391-0205 ext 102
Fax: 781-391-0315
Email: skhetani@hepregen.com

On Jan 30, 2009, at 3:35 PM, Dean.Karen@epamail.epa.gov wrote:

> Dr. Khetani, It has come to our attention that we need to ask some additional questions regarding the protection of human subjects, in the MTA that you signed back in October. The issue arose about the same time as your signing and it has taken a while to work it out with all the experts. I don't believe this will be an issue for you, but please answer the following questions and return to me as quickly as you can, so we can sign and finalize this MTA.
>
> Let me know if you have any questions. Thanks so much.
>
>
> 7. Do the Testing Results/Materials that you are providing to EPA include specimens or data derived or collected from human subjects?
> _____ Yes - Go to item #7(a).
> _____No - Skip to item #8.
>
> 7(a). Do the Testing Results/Materials include specimens or data

> derived or collected from fetuses, children, pregnant women, or
> nursing women?
> _____ Yes
> _____ No
>
> 7(b). Were the Testing Results/Materials 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?
> _____ Yes (Please indicate the applicable Regulation here
> _____ and provide copies of the protocol and IRB
> approval documents.)
> _____ No (Please provide explanation with documentary support as
> appropriate.)
>
> 7(c). Can the Provider of the Testing Results/Materials identify
> the subjects directly or through identifiers (codes) linked to
> the
> subjects?
> _____ Yes - Go to item #7(d).
> _____ No - Skip to item #8.).
>
> 7(d). Is the Provider of the Testing Results/Materials
> 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 #8.
> _____ No - Go to item #7(e).
>
> 7(e). Are the Testing Results/Materials publicly available?
> _____ Yes
> _____ No
>
> ++++++++++++++++++++++++++++++++++++
> Karen Dean
> US EPA
> National Center for Computational Toxicology
> 109 TW Alexander Drive (MD-B-205-01)
> RTP, NC 27711
>
> For commercial courier address use:
>
> 4930 Old Page Rd
> Durham, NC 27703
>
> Room B-210-K
> Phone: (919) 541-5037
> Fax: (919) 541-1194