MATERIALS TRANSFER AGREEMENT

Provider:

U.S. Environmental Protection Agency (EPA)

Office of Research and Development (ORD)

National Center for Computational Toxicology (NCCT)

Recipient:

UCLA School of Medicine

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

- **384-well plates**
- **Primary Antibody - Phospho gH2AX (rabbit) antibody**
- **Secondary Antibody - Alexa Fluor 488 antibody**
- **Propidium Iodide**
- **Bovine serum albumin**
- **Rnase A**
- **Bleomycin**
- **Etoposide**
- **Paraformaldehyde**
- **PBS**

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. Does the Research Material include specimens or data derived or collected from human subjects?

_____ Yes - Go to item #3(a).
__X___ No – Skip to item #4.

3(a). Does the Research Material include specimens or data derived or collected from fetuses, children, pregnant women, or nursing women?
_____ Yes
_____ No

3(b). Was the Research Material 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.)

3(c). Can the Provider of the Research Material identify the subjects directly or through identifiers (codes) linked to the subjects?
_____ Yes – The Recipient's use of the Research Material may be human subjects research subject to 40 CFR 26. Go to item #3(d).
_____ No – The Recipient's use of the Research Material is not human subjects research subject to 40 CFR 26. Skip to item #4.

3(d). Is the Provider of the Research Material 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 – The Recipient's use of the Research Material is not human subjects research subject to 40 CFR 26. Skip to item #4.
_____ No – The Recipient's use of the Research Material may be human subjects research subject to 40 CFR 26. Go to item #3(e).

3(e). Is the Research Material publicly available?
_____ Yes – The Recipient's use of the Research Material is human subjects research that is exempt from 40 CFR 26.
_____ No The Recipient's use of the Research Material is human subjects research that may be subject to 40 CFR 26 and must be further evaluated accordingly by the EPA Human Subjects Review Official.

4. 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 ***(insert description here or use an attachment page if necessary)***:

"Recipient" shall screen ToxCast Phase I chemicals for oncogenic effects in thyroid cells. The hypothesis behind this research is that the incidence of thyroid cancer is increasing and that this increase may be due to an environmental toxin. Recipient will provide screening data back to

"Provider".

Double strand breaks (DSB) in DNA are a precursor to the development of oncogenic mutations in cells. Non-homologous end-joining is the main pathway by which cells repair DNA DSB because it does not require a template for repair and involves limited processing of the damaged ends prior to re-ligation of the DSB. This process is more likely to result in rearrangements leading to oncogenic mutations than repair by homologous recombination. The presence of gH2AX (histone H2AX which is phosphorylated at serine 139 located in the carboxy terminal tail) is accepted as a specific indicator for the presence of DSBs.

The assay for detection of DNA DSB is an immunofluorescent method that is adapted for high throughput screening. A fast-growing functional line of thyroid cells is incubated in 384 well clear bottom plates with the environmental toxin for 24 hours. The cells are subsequently blocked with 3%bovine serum albumin/0.3% Triton X-100 and incubated with rabbit anti-phospho-H2AX antibody (Cell Signal Technologies) overnight at 4 °C. After washing, the cells are incubated with Alexa Fluor 488-labeled goat anti-rabbit antibody (Invitrogen) for 1 h at room temperature, washed, and counterstained with propidium iodide. Nuclear immune-fluorescence is visualized using the Acumen automated fluorescence microscope.

5. 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.

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. 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. Will EPA develop any products or services from information or materials provided by the Recipient?

____ Yes go to item A

X No – skip to #13 (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 (***fill-in information/material***) and will use the (***fill-in information/material***) for Agency purposes, the Recipient is required to provide EPA

with documentation such as a quality manual, describing their organization's quality system. 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

13. 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:

John Southerland
Extramural Specialist

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US EPA
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Recipient's Contact Information:

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