# MATERIALS COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT (MCRADA)

This Materials Cooperative Research and Development Agreement ("MCRADA", "Materials CRADA", or "Agreement") is entered into by and between The Brigham and Women's Hospital, Inc., a Massachusetts not-for-profit corporation which has its principal place of business at 75 Francis Street, Boston, MA 02115 ("the Collaborator"), and the Center for Computational Toxicology and Exposure ("CCTE" or "the Center"), of the U.S. Environmental Protection Agency ("EPA") under the authority of Title 15, United States Code §§ 3710a-3710d (commonly known as the Federal Technology Transfer Act of 1986).

1. Research Material.
   (a) The CCTE agrees to transfer to The Brigham and Women's Hospital, Inc., for use by the lab of Dr. Vandana Gupta ("Collaborator PI"), the following Research Material according to the Research Plan (the "Research") attached as Appendix A:

       Selected ToxCast chemical samples, up to 100 samples, and human-derived ribonucleic acid (RNA) sequencing data in the form of Transcriptomics (HTTr) data on said selected chemicals and Cell Painting (high-throughput phenotypic profiling HTTP) data on said selected chemicals, and Zebrafish developmental and behavioral RNA sequencing data on said selected chemicals.

   (b) The Brigham and Women's Hospital, Inc. agrees to transfer to the CCTE, for use by the lab of Joseph Bundy ("CCTE PI") the following Research Material:

       RNA sequencing data from Zebrafish.

   This Materials CRADA involves no other exchange of personnel or resources.

2. Human Subjects Research Ethics and Oversight. The Research Material does not involve specimens or data derived or collected from human subjects and therefore does not need review and approval by the Human Subjects Research Review Official (HSSRO).

3. Dual Use Research of Concern (DURC). The Center's DURC Internal Review Entity (IRE) has determined that this Research (as defined below) does not meet the DURC definition and that no additional review and oversight under the *USG Policy for Institutional Oversight of DURC* are required. CCTE PI must report to the IRE any

results or changes in the Research such that one or more of the 7 experimental effects of concern may apply, or if the CCTE PI feels that the Research may be DURC.

4. No Transfer. The CCTE PI and the Collaborator PI agree to retain control over the Research Materials transferred to them hereunder and further agree not to transfer the Research Material transferred to them hereunder to other people not under their direct supervision without advance written approval of the provider of said Research Material. The CCTE PI shall not use the Collaborator's Research Material received under this Agreement for any other purpose other than the Research as described in Appendix A (Appendix A is the "Research"). Collaborator PI shall not use the CCTE PI's Research Material received under this Agreement for any other purpose other than the Research. Each party reserves the right to distribute their own Research Material to others and to use it for their own purposes. When the Research Project is completed or the Materials CRADA is terminated, each party will return or destroy the Research Material of the other party at the owner's direction, to the extent such destruction is not prohibited by law.

5. Proprietary Information. The Collaborator shall place a proprietary notice on all information that it delivers to CCTE under this Agreement which it asserts is Proprietary Information of the Collaborator. CCTE agrees that: (1) any information designated as Proprietary Information which is furnished by the Collaborator to CCTE under this Agreement; (2) any information obtained by either party during the performance of this Materials CRADA that would be claimed as Proprietary Information had it been shared by the Collaborator; or (3) any information furnished by the Collaborator in contemplation of this Agreement shall be treated as Proprietary Information and will be used by CCTE only for the purpose of carrying out this Agreement. Information designated as Proprietary Information shall not be disclosed, copied, reproduced or otherwise made available in any form whatsoever to any other person, firm, corporation, partnership, association or other entity without consent of the Collaborator, except to the extent such information is required to be disclosed by the CCTE under the Freedom of Information Act (5 U.S.C. § 552) and EPA's regulations at 40 C.F.R. Part 2, or to the extent required to be disclosed by other statutes. CCTE agrees to protect the information designated as Proprietary Information from unauthorized disclosure for a period of three (3) years from the date of the disclosure and to ensure the Proprietary Information is used only by the CCTE PI and those under his supervision as necessary for the Research. The Collaborator agrees that CCTE is not liable for the disclosure of Proprietary Information which, after notice to and consultation with the Collaborator, EPA determines may not lawfully be withheld or which a court of competent jurisdiction requires to be disclosed. If no claim of confidentiality accompanies information at the time of submittal and a reasonable person would not have reason to believe such information was proprietary or of a confidential nature, then the information may be made public with no further notice

to the Collaborator.

6. No Warranty. The Research Materials are being provided hereunder as a service to the research community. THEY ARE BEING SUPPLIED TO THE RECIPIENT WITH NO WARRANTIES, EXPRESS OR IMPLIED, INCLUDING ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. The provider of the Research Material makes no representations that the use of the Research Material by the recipient will not infringe any patent or proprietary rights of third parties. CCTE shall not be liable for any claims or damages arising from the Collaborator's use of the Research Material. Collaborator shall not be liable for any claims or damages arising from the CCTE's use of the Research Material. No indemnification by either party is provided or intended.

7. Intellectual Property. Should either Party conceive and reduce to practice an invention in its performance of the Research, the Center and the Collaborator will negotiate a separate agreement with the aims of assigning responsibilities for obtaining patents or other intellectual property rights pertaining to each said invention and providing for lawful allocation of any patent or intellectual property rights resulting from each said invention. The Parties agree that each Party shall own the results of the Research that it generates ("Results"), and that each Party shall have the right to use the other Party's Results for its non-commercial research, teaching, and educational purposes. For clarity, the Research Materials are not part of the Results and ownership of Research Materials remains with the provider of each, respectively.

8. Disputes. Any dispute arising under this Agreement which cannot be readily resolved shall be submitted jointly to the signatories of this Agreement. A joint decision of the signatories or their designees shall be the suggested disposition of such dispute. If the signatories are unable to jointly resolve a dispute within a reasonable period of time after submission of the dispute for resolution, the matter shall be submitted by EPA to the Administrator of EPA or the Administrator's designee for resolution, however; nothing in this Agreement will prevent the Collaborator from pursuing other available legal recourse.

9. Severability. The illegality or invalidity of any provisions of this Materials CRADA shall not impair, affect, or invalidate the other provisions of this Materials CRADA.

10. Assignment. Neither this Materials CRADA nor any rights or obligations of any Party hereunder shall be assigned or otherwise transferred by either Party without the prior written consent of the other Party.

11. Notices. 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:

(a) If to the Collaborator:

Mass General Brigham Innovation
ATTN: Director
399 Revolution Drive, 7th Floor
Somerville, MA 02145

With a copy to:

Vandana Gupta
77 Avenue Louis Pasteur, 168A, Boston, MA 02115
617-525-4452
vgupta@research.bwh.harvard.edu

AND

TAG@mgb.org

(b) If to CCTE:

Russell Thomas
U.S. EPA Center for Computational Toxicology and Exposure (CCTE)
109 T.W. Alexander (MD-D-143-02)
Research Triangle Park, NC 27711
919.541.5776
thomas.russell@epa.gov

With a copy to:

Samantha Plishka
Extramural Management Analyst
U.S. EPA Center for Computational Toxicology and Exposure (CCTE)
109 T.W. Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919.541.2657
plishka.samantha@epa.gov

AND

Kathleen Graham
Manager
Federal Technology Transfer Act Program
1595 Wynkoop St.
Denver, CO 80202-1129
(303) 312-6137
graham.kathleen@epa.gov

Either party may change the contact information set out above by notice given to the other party in the manner set forth above.

12. No Endorsement. By entering into this Materials CRADA, neither CCTE nor the Collaborator directly or indirectly endorses any product or service provided, or to be provided, whether directly or indirectly related to either this Materials CRADA or to any patent or other intellectual property license or agreement which is related to this Materials CRADA. The Collaborator shall not in any way state or imply that this Materials CRADA is an endorsement by the U.S. Government or any of its organizational units or employees of any such product or service. CCTE shall not in any way state or imply that this Materials CRADA is an endorsement by The Brigham and Women's Hospital, Inc. or any of its organizational units or employees of any such product or service.

13. Termination. Either the Center or the Collaborator may unilaterally terminate this entire Agreement at any time by giving written notice to the other party at least thirty (30) days prior to the desired termination date.

14. Entire Agreement. This Materials CRADA constitutes the entire agreement between the Parties with respect to this subject matter and supersedes any prior understanding or written or oral agreement with respect to this subject matter.

15. Governing Law. This Materials CRADA shall be construed in accordance with Federal law as applied by the Federal courts in the District of Columbia.

16. Power and Authority. The undersigned expressly certify and affirm that the contents of any respective statements made or reflected in this Materials CRADA are truthful and accurate to the knowledge of the undersigned, respectively, and that the signatories hereto have the authority to bind their respective organizations to this agreement.

17. Effective Date. This Materials CRADA shall be effective upon execution by the Parties

when the last signatory has signed the document.

18. Duration. The term of this Materials CRADA is 36 months from execution.

19. The provisions of Articles 3, 4, 5, 6, 7, 8, 9, and 15 shall survive the termination of this Materials CRADA.

**IN WITNESS WHEREOF**, the Parties have caused this Agreement to be executed by their duly authorized representatives as follows:

**For CCTE:**

By: [redacted]

# APPENDIX A

## RESEARCH PLAN

Dr. Gupta is an expert in the area of rhabdomyolysis, a serious health condition in which muscle breaks down in response to chemical or physical stress, leading to serious effects including kidney damage. The experimental techniques used in the Gupta lab include transcriptomics on human cell lines and zebrafish and other zebrafish-related assays. The CCTE is developing high-throughput methods for performing transcriptomics (HTTr), cell-based phenotypic profiling (HTPP) and zebrafish developmental and behavioral assays. The CCTE is developing these methods to help discover environmental chemicals that can lead to toxic outcomes such as rhabdomyolysis. Additionally, the CCTE has already generated data on >1000 chemicals in each of its assays, and this data could be used to identify candidate rhabdomyolysis causing chemicals.

Specific research activities will or may include:
1. Months 1-2: CCTE and Dr. Gupta's lab will agree upon and document in writing the selected ToxCast chemical samples, up to 100 samples, that CCTE will transfer to Dr. Gupta. CCTE will provide Dr. Gupta's lab with the results of HTTr, HTPP and zebrafish assays already generated.

2. Months 3-6: CCTE will provide Dr. Gupta's lab with samples of specified ToxCast chemicals.

3. Months 7-18: Dr. Gupta's lab will conduct transcriptomics and zebrafish studies on these ToxCast chemicals to determine specific molecular or phenotypic signatures related to rhabdomyolysis.

4. Months 19-24: The CCTE may run specific compounds in HTTr, HTPP or zebrafish assays to confirm or extend the results obtained for these compounds in Dr. Gupta's lab.

5. Months 25-30: The CCTE will provide information on chemicals causing rhabdomyolysis related symptoms in mammalian species, using data from ToxRefDB.

6. Months 31-36: As appropriate the two groups will co-publish on the results of this research.