

**COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
WITH THE
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**

This Cooperative Research and Development Agreement (“CRADA” or “Agreement”) is entered into by and between Dr. Johanna Nyffeler (“the Cooperator”), and the Center for Computational Toxicology and Exposure (CCTE) (“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).

WITNESSETH:

A. WHEREAS, the Congress, in enacting the Federal Technology Transfer Act of 1986 (the “FTTA”), has found that Federal laboratories’ developments should be made accessible to private industry, state and local governments, and has declared that one of the purposes of such Act is to improve the economic, environmental and social well-being of the United States by stimulating the utilization of Federally-funded technology developments by such parties;

B. WHEREAS, the FTFA provides each Federal agency with the authority to permit the Directors of Government-operated laboratories to enter into cooperative research and development agreements with Federal or non-Federal entities, including private firms and organizations for the purpose of providing to, or obtaining from, collaborating parties, personnel, services, property, facilities, equipment, intellectual property or other resources toward the conduct of specified research and development efforts, which may include the disposition of patent or other intellectual property rights in the inventions resulting from such collaboration;

C. WHEREAS, the Center has performed and has sponsored substantial research and development with respect to computational and predictive toxicology;

D. WHEREAS, the Center possesses certain advanced scientific skills, facilities, special equipment, information, computer software, and know-how pertaining to the development of new alternative approaches, including in vitro assays and computational approaches, for chemical safety screening;

E. WHEREAS, the Cooperator possesses certain expertise in development of new alternative approaches, in particular high-throughput phenotypic profiling, and the data analysis thereof;

F. WHEREAS, the Center and the Cooperator are interested in the further research and development of the high-throughput phenotypic profiling technology and its utilization for chemical safety screening;

G. WHEREAS, the Cooperator desires to provide resources for the Center’s development and/or evaluation of the high-throughput phenotypic profiling technology with respect to using a human neuronal cell model and animal-free culture conditions; and

H. WHEREAS, the Center views its collaboration with the Cooperator to develop and evaluate the use of a human neuronal cell model for chemical safety screening using high-throughput phenotypic profiling technology to be in the furtherance of the public interest.

NOW, THEREFORE, the parties hereto agree as follows:

Article 1. Definitions

As used in this CRADA, the following terms shall have the following meanings and such meanings should be equally applicable to both the singular and plural forms of the terms defined:

1.1 “CRADA” or “Agreement” means this Cooperative Research and Development Agreement entered into by the Center pursuant to 15 U.S.C. § 3710a.

1.2 “Computer Software” means computer software, computer programs, computer data bases, and documentation thereof developed, in whole or in part, under this Agreement.

1.3 “Government” means the Government of the United States of America.

1.4 “Invention” means any invention or discovery which is or may be patentable or otherwise protectable under the intellectual property laws of this or any foreign country.

1.5 “Made” in relation to any Invention means the conception or first actual reduction to practice of such Invention.

1.6 “Proprietary Information” means information which embodies trade secrets developed at private expense, or which is confidential scientific, business, or financial information, provided that such information:

(a) Is not generally known or available from other sources without obligation concerning its confidentiality;

(b) Has not been made available by the owners to others without obligation concerning its confidentiality; and

(c) Is not already available to the Government without obligation concerning its confidentiality.

1.7 “Subject Data” means all recorded information first produced in the performance of this Agreement. This term includes Computer Software.

1.8 “Subject Invention” means any Invention conceived or first actually reduced to practice in the performance of work under this Agreement.

1.9 “Technology” means high-throughput phenotypic profiling, including associated computer software, programs, data bases, and documentation.

1.10 “Works” means any Computer Software or subject matter that is copyrightable.

Article 2. Cooperative Research

2.1 Statement of Work. Cooperative research and development work performed under this Agreement shall be performed in accordance with the Statement of Work (“SOW”) attached hereto as Attachment A. The SOW sets forth a “period of performance.” The Center and the Cooperator agree to perform the cooperative research and development work and to utilize such personnel, resources, facilities, equipment, skills, know-how and information as is reasonably necessary.

2.2 Review of Work. Periodic meetings shall be held between Center and Cooperator personnel for the purpose of reviewing the progress of the work to be accomplished under this Agreement. The Center shall have exclusive control and supervision over the conduct of all cooperative research and development work conducted at the Center facilities. It is understood that the nature of this cooperative research and development work is such that completion within the period of performance specified in the SOW or within the limits of financial support allocated, cannot necessarily be guaranteed. Accordingly, it is agreed that all cooperative research is to be performed on a best-efforts basis.

2.3 Assigned Personnel. Each party to this Agreement shall perform its respective obligations under this Agreement under the direction of a “Project Manager” and a “Principal Investigator”. Project Managers shall be responsible for the overall direction of the work, establishing budgets and providing such approvals and consents as are required hereunder. Principal Investigators shall be responsible for the scientific and technical conduct of the work, including the exchange of Subject Data and other information. The parties designate the following individuals as their respective representatives:

	<u>Center</u>	<u>Cooperator</u>
Project Manager	Sandra Roberts	Johanna Nyffeler
Principal Investigator	Joshua Harrill	Johanna Nyffeler

2.4 Scope Change. If at any time the Project Manager determines the research data justifies a substantial change in the direction of the work, the parties shall make a good faith effort to agree on any necessary changes to the SOW.

Article 3. Reports

3.1 Final Report. The Center and Cooperator shall jointly prepare and submit a final report to the Center Director of the data for use in a publication after (a) completing the SOW or (b) the termination of this Agreement.

Article 4. Financial Obligations

4.1 Transfer of Funds. The Cooperator agrees to pay eight thousand dollars (\$8,000) to EPA for the performance of research specified in Article 2 and the SOW in Attachment A. Funds must be received by the Center before work can be initiated.

4.1.1 Payment by Check. A check payable to the U.S Environmental Protection Agency (EPA) may be used as payment of funds. The check (made payable to U.S. Environmental Protection Agency) shall be mailed to:

U.S. Environmental Protection Agency
FOIA and Miscellaneous Payments
Cincinnati Finance Center
P.O. Box 979078
St. Louis, MO 63197-9000

The check shall be accompanied by a copy of the first page of this Agreement, the signature page of this Agreement, and the SOW in Attachment A.

4.1.2 Payment by Wire Transfer. Wire transfers should be directed to the Federal Reserve Bank of New York

Federal Reserve Bank of New York
ABA = 021030004
Account = 68010727
SWIFT address = FRNYUS33
33 Liberty Street
New York NY 10045
Field Tag 4200 of the Fedwire message should read "D 68010727
Environmental Protection Agency"

4.2 Assignment of Personnel. EPA will assign personnel as necessary to complete this project. In addition to the funding by the Cooperator provided for in paragraph 4.1 above, the Cooperator will personally provide qualified research services to perform the efforts under the SOW in Appendix A. The Cooperator will be stationed at the EPA facility in Research Triangle Park.

4.3 Use of Funds. EPA shall ensure that all amounts paid by or on behalf of the Cooperator pursuant to this CRADA shall be used exclusively for the conduct of the SOW by the Center under and in accordance with the terms of this CRADA. The funds cannot be used to purchase any products of non-human animal origin.

4.4 Accounting Records. The Center shall maintain separate and distinct current accounts, records, and other evidence supporting all its expenditures of the Cooperator's cash contributions under this Agreement. The accounts and records shall be available for reasonable inspection and copying by the Cooperator or its authorized representative.

Article 5. Subject Inventions and Patent Rights, Computer Software, and Copyright.

5.1 Reporting. The Center and the Cooperator acknowledge that it is not their intention that Subject Inventions or Computer Software will be created during the work specified in this Agreement. Notwithstanding the foregoing, where any activity of this Agreement results in the creation of Subject Inventions or Computer Software, the parties agree that all right, title, and interest in and to all Subject Inventions or Computer Software shall, regardless of inventorship, vest in and be the sole property of inventing party, subject to the terms hereof.

5.2 Jointly Owned Works. The parties agree that for any Subject Inventions or Computer Software that are jointly owned pursuant to section 5.1, the Center and the Cooperator will negotiate in good faith an amendment to this Agreement that shall include assignment of responsibilities for obtaining patents or other intellectual property rights pertaining to the Subject Inventions or Computer Software.

5.3 Subject Inventions. The Center, on behalf of the U.S. Government, hereby grants to the Cooperator a first option to an exclusive license of the Government's interest in each Subject Invention and in any resulting patents that issue on such Subject Inventions. This option must be exercised not later than six (6) months following the filing of a patent application in the U.S. Patent and Trademark Office or under the Patent Cooperation Treaty. Any exclusive license granted by the Center shall be subject to the reservation by the U.S. Government of a nonexclusive, nontransferable, irrevocable paid-up license to practice or have practiced on its behalf the Subject Invention throughout the world, in accordance with 15 U.S.C. §3710a(b)(1).

5.4 Jointly Created Works. The parties agree that any copyrightable subject matter created jointly by the parties from the activities conducted under this Agreement may be copyrighted by the Cooperator. Further, if the Cooperator intends to disseminate the Work(s) outside of the United States, Cooperator may secure copyright to the extent authorized under the domestic laws of the relevant country. If the Cooperator asserts copyright to jointly developed Works, Cooperator hereby grants to the U.S. Government and others acting on its behalf a nonexclusive, irrevocable, paid-up worldwide license in such copyrighted Works to use, reproduce, distribute, publish, prepare derivative works, perform publicly, and display publicly the Works.

Article 6. Data and Publication

6.1 Proprietary Information. The Cooperator shall place a proprietary notice on all information it delivers to the Center under this Agreement which it asserts is Proprietary Information of the Cooperator. The Center agrees that: 1) any information designated as Proprietary Information which is furnished by the Cooperator to the Center under this Agreement; 2) any information obtained by either party during the performance of this CRADA that would be claimed as Proprietary Information had it been submitted by the Cooperator; or 3) any information furnished by the Cooperator in contemplation of this Agreement; shall be treated as Proprietary Information and will be used by the Center only for the purpose of carrying out this Agreement or for Government purposes. 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 Cooperator except as such information may be subject to disclosure under the Freedom of Information Act (5 U.S.C. § 552), and EPA's regulations at 40 C.F.R. Part 2, or as required to be disclosed by other statutes. The Center agrees to use its best efforts to protect the information designated as Proprietary Information from unauthorized disclosure. The Cooperator agrees that the Center is not liable for the disclosure of Proprietary Information which, after notice to and consultation with the Cooperator, 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 Cooperator.

6.2 Release Restrictions. The Center shall have the right to use all Subject Data for any Governmental purpose; provided, however, that the Center shall not release such Subject Data publicly or provide such Subject Data to any Government regulatory body or agency other than the EPA except:

(a) the Center in reporting the results of cooperative research may publish Subject Data, subject to the provisions of paragraph 6.3 below, and provided the Cooperator is given 45 days to review the manuscript and provide suggestions before publication;

(b) the Center may release such Subject Data where such release is required pursuant to a request under the Freedom of Information Act (5 U.S.C. § 552) and the EPA regulations at 40 C.F.R. Part 2 or as required to be disclosed by other statutes;

(c) The Cooperator agrees to not release any Subject Data without obtaining prior written consent from the Center; and

(d) Pursuant to 35 U.S.C. § 205, neither the Center nor the Cooperator shall release to the public any Subject Data or other data that discloses or enables an invention if a patent application is to be filed, until the party having the right to file a patent application or provisional patent application has had a reasonable time to file.

6.3 Publication. The Center and the Cooperator agree to confer and consult prior to the publication of Subject Data to ensure that no Proprietary Information is released and that patent rights are not jeopardized. Prior to submitting a manuscript for outside review which contains the results of the research under this Agreement, or prior to publication if no such review is made, each party shall be offered at least 45 calendar days to review such proposed publication and to file patent applications in a timely manner, if it is so entitled or required under this Agreement.

Article 7. Representations and Warranties

7.1 Representation and Warranties of the Center. The Center hereby represents and warrants to the Cooperator as follows:

7.1.1 Organization. The Center is a Federal Laboratory of the EPA and is wholly owned by the Government. The Center's substantial purpose is the performance of research and development.

7.1.2 Mission. The performance of the activities specified by this Agreement is consistent with the mission of the Center.

7.1.3 Authority. All prior reviews and approvals required by Federal regulations and laws have been obtained by the Center prior to the execution of this Agreement. The Center official executing this Agreement has the requisite authority to do so.

7.2 Representations and Warranties of the Cooperator. The Cooperator hereby represents and warrants to the Center as follows:

7.2.1 Corporate Organization. The Cooperator is a natural person and is a recipient of the Young Researcher Lush Prize (www.lushprize.org). The Cooperator agrees all research performed at the Center laboratory will be performed with an EPA mentor present.

7.2.2 Power and Authority. The Cooperator has the requisite power and authority to enter into this Agreement and to perform according to the terms thereof.

7.2.3 No Violation. The execution and delivery of this Agreement do not contravene any material provision of, or constitute a material default under, any material agreement binding on the Cooperator or any valid order of any court, or any regulatory agency or other body having authority to which the Cooperator is subject, nor, to the best of its knowledge, is the Cooperator the subject of any adversarial proceeding by any regulatory governmental agency.

Article 8. Termination

8.1 Termination by Mutual Consent. The Center and the Cooperator may elect to terminate this Agreement, or portions thereof, at any time by mutual consent. In such event the parties shall specify the disposition of all property, patents, unexpended or unobligated funds, and the results arising from the work completed or in progress under this Agreement. Upon termination by mutual consent, the Center, as of the termination date, shall make no new commitments, and as soon after the termination date as feasible, shall cancel all outstanding commitments that relate to those portions of this Agreement that have been mutually terminated.

8.2 Termination by Unilateral Action. Either party may unilaterally terminate this entire Agreement at any time by giving the other party written notice not less than thirty (30) calendar days prior to the desired termination date. The Center shall make no new commitments after receipt of a written termination notice from the Cooperator and shall to the extent possible, by the termination date, cancel all outstanding commitments and contracts that were entered into as a consequence of the requirements of the SOW in Attachment A. However, the Center may, at its

own expense, continue said commitments beyond said termination date without liability on the part of the Cooperator.

8.3 Termination Costs. Each party shall pay its own termination costs out of its own funds. Any funds furnished by the Cooperator which are unexpended or unobligated as of the date of termination will be returned to the Cooperator. In no event shall either party be liable for the direct and indirect termination costs of the other party or said other party's expenses caused by or related to the termination.

8.4 Survival. To the extent rights and obligations hereunder have accrued as of the date of expiration or termination, the following Articles of this Agreement shall survive any expiration or termination hereof: 5, 6, and 10, and any expiration or termination hereof shall not affect any license granted hereunder.

Article 9. Disputes

9.1 Settlement. 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 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 to the Administrator of EPA or the Administrator's designee for resolution.

9.2 Continuation of Work. Pending the resolution of any dispute or claim pursuant to this Article, the parties agree that performance of all obligations shall be pursued diligently in accordance with the direction of the Center signatory.

Article 10. Liability

10.1 EPA. EPA's responsibility for the payment of claims to the Cooperator or its employees for loss of property, personal injury or death caused by the negligence or the wrongful act or omission of employees of EPA, while acting within the scope of their employment, is in accordance with the provisions of the Federal Tort Claims Act, 28 U.S.C. §§ 2671-80 and 40 C.F.R. Part 10.

10.2 No Warranty. Except as specifically stated in Article 7, neither party makes any express or implied warranty as to any matter whatsoever, including the conditions of the research or as to any Invention made or product developed, or the ownership, merchantability, or fitness for a particular purpose, of the research or any such Invention or product.

10.3 Indemnification. The Cooperator agrees to hold the Government harmless and to defend and indemnify the Government for all liabilities, demands, damages, expenses and losses arising out of the use by the Cooperator, its employees or any party acting on the Cooperator's behalf or with its authorization, of the Center's research and technical developments, the Center's facilities or equipment, or out of any use, sale or other disposition by the Cooperator, its employees

or others acting on its behalf or with its authorization, of products made by the use of the Center's technical developments. This provision shall survive the termination of this Agreement.

10.4 Force Majeure. Neither party shall be liable for any event or circumstance beyond its reasonable control not caused by the fault or negligence of such party, which causes such party to be unable to perform its obligations under this Agreement (and which it has been unable to overcome by the exercise of due diligence), including but not limited to flood, drought, earthquake, storm, fire, pestilence, lightning and other natural catastrophes, epidemic, war, riot, civil disturbance or disobedience, strikes, labor dispute, sabotage of the Center facilities, or any order or injunction made by a court or public agency. In the event of the occurrence of such a force majeure event, the party unable to perform shall promptly notify the other party. It shall further use its best efforts to resume performance as quickly as possible and shall suspend performance only for such period of time as is necessary as a result of the force majeure event.

10.5 Cooperator. The Cooperator agrees that during the term of this Agreement it will carry liability insurance in the amount set forth on the attached certificate of insurance to cover any liability to the Government or to Government employees and private individuals that may arise as a result of negligent acts or omissions of any of the Cooperator's employees or agents while they are performing work under this Agreement including any work which such employee or agent may be performing at the Laboratory.

Article 11. Miscellaneous

11.1 No Benefits. No member of, or delegate to the United States Congress, or resident commissioner, shall be admitted to any share or part of this Agreement, nor to any benefit that may arise therefrom. This provision shall not be construed to extend to this Agreement if the Agreement is made with the Cooperator for the Cooperator's general benefit.

11.2 Governing Law. The construction, interpretation, validity, performance, and effect of this Agreement for all purposes shall be governed by the laws applicable to the federal government.

11.3 Headings. Titles and headings of the Sections and Subsections of this Agreement are for the convenience of references only and do not form a part of this Agreement and shall in no way affect the interpretation thereof.

11.4 Waivers. None of the provisions of this Agreement shall be considered waived by any party hereto unless such waiver is given in writing to all other parties. The failure of any party to insist upon strict performance of any of the terms and conditions hereof, or failure or delay to exercise any rights provided herein or by law, shall not be deemed a waiver of any rights of any party hereto.

11.5 Severability. The illegality or invalidity of any provisions of this Agreement shall not impair, affect, or invalidate the other provisions of this Agreement.

11.6 Amendments. If either party desires a modification to this Agreement, the parties shall, upon reasonable notice of the proposed modification by the party desiring the change, confer in good faith to determine the desirability of such modification. Such modification shall not be effective until a written amendment is signed by all the parties hereto by their representatives duly authorized to execute such amendments.

11.7 Assignment. Except as otherwise permitted herein, neither this Agreement 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. However, the Cooperator may assign this Agreement to the successors or assignees of a substantial portion of the Cooperator's business interests to which this Agreement directly pertains.

11.8 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 or sent by certified mail, return receipt requested, with postage prepaid, addressed as follows:

(a) If to CENTER:

Authorized Representative (signator)

Russell Thomas
Center for Computational Toxicology and Exposure (CCTE)
US EPA
109 TW Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-5776
thomas.russell@epa.gov

With a copy to (other):

Samantha Plishka
Program Manager
Center for Computational Toxicology and Exposure (CCTE)
US EPA
109 TW Alexander (AA005)
Research Triangle Park, NC 27711
919-541-2657
plishka.samantha@epa.gov

AND

Sandra Roberts
Project Manager
Center for Computational Toxicology and Exposure (CCTE)
Biomolecular and Computational Toxicology Division (BCTD)
US EPA
109 TW Alexander (MD-B-205-01)

EPA-Nyffeler CRADA #1310-20

Research Triangle Park, NC 27711
919-541-3850
roberts.sandra@epa.gov

AND

Joshua Harrill
Principal Investigator
Center for Computational Toxicology and Exposure (CCTE)
Biomolecular and Computational Toxicology Division (BCTD)
US EPA
109 TW Alexander (MD-B205-01)
Research Triangle Park, NC 27711
919-541-0646
Harrill.joshua@epa.gov

AND

FTTA Program Coordinator:

Kathleen Graham
graham.kathleen@epa.gov
(303) 312-6137
FTTA@epa.gov

(b) If to COOPERATOR:

Authorized Representative (signator)

Johanna Nyffeler,
1101 Exchange Pl, Apt 732
Durham, NC, 27713
(336) 538 3214
johanna.nyffeler@swissonline.ch

Any party may change such address by notice given to the other party in the manner set forth above.

11.9 Independent Parties. The relationship of the Center and the Cooperator is that of independent parties and not as agents of each other or as joint venturers or partners. The Center shall maintain sole and exclusive control over its personnel and operations. The Cooperator acts as a sole and exclusive entity.

11.10 Use of Name or Endorsements. The Cooperator shall not use the name of the Center or EPA, on any product or service which is directly or indirectly related to either this Agreement or any patent license or assignment agreement which implements this Agreement, without the prior approval of the Center. By entering into this Agreement, the Center does not directly or indirectly

endorse any product or service provided, or to be provided, by the Cooperator, its successors, assignees, or licensees. The Cooperator shall not in any way imply that this Agreement is an endorsement of any such product or service. This section in no way prohibits the publication of any EPA indication or statement regarding the efficacy of any Subject Invention and/or any other results of this Agreement.

11.11 No Approval. Nothing in this Agreement shall be deemed to constitute regulatory or scientific approval of the use of any particular product or technology. The Cooperator agrees that (a) nothing in this Agreement relieves it of any obligation to comply with applicable federal, state, or local laws, regulations, or requirements, and (b) possession or acquisition by the Center of Subject Data, or other information generated or otherwise acquired pursuant to performance of work under this Agreement, does not constitute knowledge of or possession or receipt of such data or information by or on behalf of the Administrator of the Environmental Protection Agency for purposes of statutory or regulatory reporting requirements such as, but not limited to, Section 8 of the Toxic Substances Control Act.

11.12 Entire Agreement. This Agreement constitutes the entire agreement between the parties concerning the subject matter hereof and supersedes any prior understanding or written or oral agreement relative to said matter.

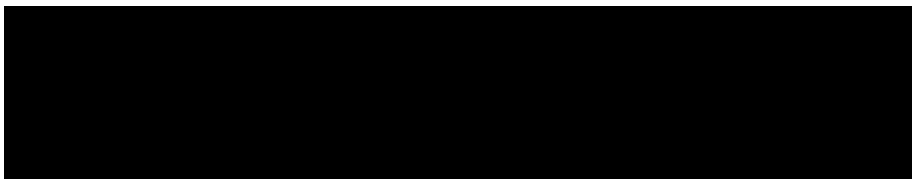
Article 12. Duration of Agreement and Effective Date

12.1 Effective Date. This Agreement shall enter into force as of the date of the last signature of the parties.

12.2 Duration. This Agreement shall remain in effect for a period of two (2) years from the effective date.

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

U.S. ENVIRONMENTAL PROTECTION AGENCY



Date _____

THE COOPERATOR

