COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT WITH THE UNITED STATES ENVIRONMENTAL PROTECTION AGENCY AND UNILEVER GLOBAL IP LIMITED

This Cooperative Research and Development Agreement ("CRADA" or "Agreement") is entered into by and between **UNILEVER GLOBAL IP LIMITED**, a company incorporated in England and Wales (registered under number 12920301) and whose registered office is at Port Sunlight, Wirral, Merseyside, CH62 4ZD, UK ("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 FTTA 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 non-animal based new approach methods (NAMs);

E. WHEREAS, the Cooperator possesses certain expertise in chemical risk assessment of consumer products, in vitro assays, metabolism, and exposure;

F. WHEREAS, the Center and the Cooperator are interested in the further research and development of non-animal based NAMs for evaluating the safety and hazard of chemicals, establishing Next Generation Risk Assessments (NGRA) technology and its utilization by private and public entities;

G. WHEREAS, the Cooperator desires to provide resources for the Center's development and/or evaluation of the NAM technology; and

H. WHEREAS, the Center views its collaboration with the Cooperator to develop/evaluate the NAM 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 "Affiliates" means, in the case of the Cooperator, the companies of the Unilever Group controlled, directly and indirectly, by Unilever PLC in London.

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

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

1.4 "Government" means the Government of the United States of America.

1.5 "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.

1.6 "Made" in relation to any Invention means the conception or first actual reduction to practice of such Invention.

1.7 "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.

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

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

1.10 "Technology" means ToxCast™, its databases and documentation, non-animal based New Approach Methods (NAM), Next Generation Risk Assessment (NGRA) and modeling.

1.11 "Works" means any Computer Software or subject matter that is copyrightable.

1.12 "Permitted Human Cells or Tissues" means cells or tissues purchased at arm's length on any regulated marketplace from a registered commercial entity, excluding use of embryonic stem cells.

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 conferences 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. The Cooperator shall have exclusive control and supervision over the conduct of all cooperative research and development work conducted at Cooperator 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 effort 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:

	Center	Cooperator
Project Manager	Richard Judson	Paul Carmichael/Matthew Dent
Principal Investigator	Josh Harrill	Sharon Scott/Geoff Hodges

2.4 Scope Change. If at any time the Project Managers determine that the research data justify 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. Any change shall be effective only if agreed in writing by the Cooperator signed by its officer having authority therefor.

Article 3. Reports

3.1 Final Report. The Center shall submit a final report to the Cooperator of the results within ninety (90) calendar days after (a) completing the SOW or (b) the termination of this Agreement. The Cooperator shall submit a final report to the Center of the Cooperator's results within ninety (90) calendar days after (a) completing the SOW or (b) the termination of this Agreement. A progress report will be due from the Cooperator at the end of Year 1 and Year 2, with milestone payments associated.

Article 4. Financial Obligations

4.1 Transfer of Funds. Annex 1 Part 1 sets forth the Cooperator's Total Funding Commitment that Cooperator agrees to pay to the Center pursuant to this Agreement. Annex 1 Part 1 also sets forth the maximum amounts EPA agrees to spend for each identified Task and other expenses over the course of the Agreement. The Cooperator will pay the Center the amounts listed in and according to the schedule set forth in Annex 1, Part 2. The Cooperator will pay the Center in advance of each phase of work provided that substantial progress on the work as set forth in the SOW has occurred. Such payments shall be exclusive of value added tax, sales tax, or equivalent point of sale or service tax. Payments to the Center shall be made to the USEPA via electronic transfer.

4.2 Invoicing. The Center agrees to submit invoices to the Cooperator in the amounts listed in Annex 1, Part 2, at the time of the Milestones listed therein. Invoices must comply with the invoicing requirements set out at www.unileversuppliers.com. All invoices shall quote the (i) project reference number **MA-2020-00690N** and the (ii) purchase order number **PO12349954** and be addressed to:

Unilever R&D Colworth,
UK Accounts Payable,
Mail-Point 13598,
Unit B Rattys Lane,
Hoddesdon,
Hertfordshire,
EN11 0RF.

Where the Cooperator disputes in good faith any invoice, the Cooperator is entitled to withhold payment in the disputed amount from the next phase's payment without penalty until the dispute is resolved. In such instance, the parties will confer regarding the status of the work, and make any necessary amendments to the SOW or this Agreement.

Except as stated above, each Party is responsible for its own costs of performing this Agreement. The Cooperator has no other obligation to make any payment of charges, fees, or costs in respect of the performance of this Agreement.

The Cooperator will not provide funding for any work outside the scope of the SOW unless the Cooperator has agreed in writing, in advance of performance.

4.3 Assignment of Personnel. In addition to the funding by the Cooperator provided for as documented in the SOW, the Cooperator shall provide the services of a qualified research associate who will assist in the efforts under the SOW in Appendix A. The associate shall be an employee of the Cooperator and shall be stationed at Unilever, SEAC, Sharnbrook, United Kingdom. The parties acknowledge their intention that any persons provided by the Cooperator are also to receive training in the use of the Technology coordinated by the Center's Principal Investigator, either remotely or at the Center's facility.

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. The Center will provide a yearly spreadsheet accounting for the funds spent.

4.5 No Further Payments by the Cooperator. The Cooperator shall have no obligation to make any payment hereunder, save as expressly provided by the terms of Section 4.1 of this Agreement. For clarity, the SOW shall impose no obligation upon the Cooperator to make any payment hereunder.

Article 5. Invention, Computer Software, and Patent Rights

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 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 hereunder 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. 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, prepare derivative works, perform publicly, and display publicly the Work.

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, its staff or its Affiliates 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, then the information may be made public with no further notice to the Cooperator.

Prompt written notice of such requirement of disclosure shall be given to the Cooperator so that it may endeavor to obtain appropriate relief to prevent or limit such disclosure. The Center shall disclose information, where it is lawful for the Center to do so and only as and to the extent required by said administrative requirement or court order, and such disclosure shall not of itself be prejudicial to any of the other confidentiality obligations hereunder.

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 in accordance with the provisions of paragraph 6.3 below; and

(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;

(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 have an objective to publish and disseminate research results. Where the Center or the Cooperator ("Publishing Party") intend to publish Subject Data, the Publishing Party shall ensure that the other of the Center or the Cooperator ("Reviewing Party") shall have been furnished with copies of any proposed publication or presentation of Subject Data or other information arising from the SOWs in a timely manner, being at least forty five (45) days, in advance of their submission to any third party. The Reviewing Party shall notify the Publishing Party within said 45-day period of any Proprietary Information contained in the proposed publication. The Center and the Cooperator agree to confer and consult within said 45 day period prior to the publication to reach agreement between the parties that no Proprietary Information is released and that patent rights or trade secrets are not jeopardized, before the Publishing Party may proceed to publication.

Article 7. Representations and Warranties

7.1 Representation and Warranties of the Laboratory. 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 or 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, as of the date hereof, is a corporation duly organized, validly existing, and in good standing under the laws of the United Kingdom.

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 Due Authorization. The Board of Directors and stockholders of the Cooperator have taken all actions, if any, required to be taken by law, the Cooperator's Certificate or Articles of Incorporation, its bylaws or otherwise, to authorize the execution and delivery of this Agreement.

7.2.4 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 ninety (90) 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 Center. For clarity, said liability insurance coverage includes any policy of self-insurance.

10.6. Indirect Damages. The parties agree that in no event shall any party be liable for any pure economic loss, special, exemplary, incidental or consequential damages arising under or pursuant to this Agreement, even if said party, their Affiliates or their employees have been advised of the possibility of, should have known of, or could reasonably have prevented, such damages.

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, Ph.D.
Director, Center for Computational Toxicology & Exposure (CTTE)
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:
Samantha Plishka
Center Program Coordinator
Center for Computational Toxicology & Exposure (CTTE)
US EPA
109 TW Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-2657
plishka.samantha@epa.gov

AND

Richard Judson
Project Manager
Center for Computational Toxicology & Exposure (CTTE)
Biomolecular & Computational Toxicology Division (BCTD)
US EPA
109 TW Alexander (MD-B-205-01)
Research Triangle Park, NC 27711
919-541-3085
judson.richard@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):
Julia Fentem, Vice President
Unilever, Safety and Environmental Assurance Centre (SEAC)
Colworth Science Park
Sharnbrook
Bedfordshire MK44 1LQ
United Kingdom
julia.fentem@unilever.com

With a copy to:
Andrew Scott
Unilever, Safety and Environmental Assurance Centre (SEAC)
Colworth Science Park
Sharnbrook
Bedfordshire MK44 1LQ
United Kingdom
andrew.scott@unilever.com

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 shall maintain sole and exclusive control over its personnel and operations.

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 or Computer Software 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 Human Subjects (if applicable). The Cooperator agrees to comply with all applicable provisions of EPA Regulation 40 CFR 26 **(Protection of Human Subjects)**. This includes, at Subpart A, the Basic Federal Policy for the Protection of Human Research Subjects, also known as the Common Rule. It also includes, at Subparts B, C, and D, prohibitions and additional protections for children, nursing women, pregnant women, and fetuses in research conducted or supported by EPA. The Cooperator further agrees to comply with EPA's procedures for oversight of the Cooperator's compliance with 40 CFR 26, as given in EPA Order 1000.17 Change A1 **(Policy and Procedures on Protection of Human Research Subjects in EPA Conducted or Supported Research)**.

11.13 Animal Testing. The Center shall ensure that, in the conduct of the SOW, there shall be no use of any Animals and no use of Animals to provide tissues, cells or specific reagents, where "Animal" means any non-human vertebrate or cephalopod. The foregoing does not prohibit use of standard, immortalized animal-derived cell lines and off-the-shelf laboratory reagents that are generally available from commercial suppliers.

11.14 Permitted Human Cells or Tissues. The Center shall ensure that, in the conduct of the SOW, there shall be no human testing or use of any humans, cell lines, or any human tissues, except the Permitted Human Cells or Tissues, without prior written consent from the relevant Unilever R&D VP or EVP to ensure that it complies with Unilever policies and standards (e.g., Ethical Review of Research on Human Subjects). On written request, the Center shall provide to Unilever written evidence of its compliance with the foregoing.

11.15 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 three (3) 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.

Annex 1 - Financial Summary

Part 1: Level of Funding

The Cooperator's total funding commitment under this Agreement shall not exceed the following amount:

The Cooperator Total Funding Commitment pursuant to this Agreement	$2,084,000

Said amount shall be allocated to the following cost headings:

Item	Funding
Task 1: Selection of Chemicals	$25,000
Task 4: Addition of metabolic capacity to one cell line for use in HTTr and HTPP	$10,000
Task 5: Run HTTr in 12 cell lines **Sequencing –** **Technician Support -**	$1,091,000 $160,000
Task 6: Run HTPP in 12 cell lines	$42,000
Task 7: Run assays required for toxicokinetics (TK)	$264,000
Task 8: Run in vitro disposition measurements	$45,000
Task 9: Metabolite determination	$165,000
Task 11: Cross-species extrapolation	$255,000
Travelling and other expenses (excluding VAT)	$27,000
Total (excluding VAT)	$2,084,000

The foregoing shall include all travelling and other expenses as may be incurred by the Center and/or its staff connected with the SOWs.

Part 2: Payment Details

Subject to the conditions set forth in the Agreement, the Cooperator shall make payment pursuant to clause 4 as follows:

Expected date	Phase to be funded - Milestone	Funding for next phase
Start of Project	Start of Project	$694,666.66
One year after Effective Date	Progress report for Year 1 (Tasks 1 – 11)	$694,666.66
Two years after Effective Date	Progress report for Year 2 (Tasks 1 – 11)	$694,666.68
Total		**$2,084,000**

STATEMENT OF WORK

COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT
WITH THE
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
AND
UNILEVER GLOBAL IP LIMITED

Title of Project: Development and Evaluation of New Approach Methods (NAMs) in the Origination of Next Generation Risk Assessments (NGRA)

The Goal:
The goal of this CRADA is to jointly explore the utility of a battery of new approach methods (NAMs), which are non-animal based, for evaluating the safety and hazard of chemicals – establishing Next Generation Risk Assessments (NGRA). One of the primary missions of the CCTE is to develop such methods, including high-throughput screening (HTS), under the long-running ToxCast project. This includes high-throughput toxicokinetics (HTTK), high-throughput transcriptomics methods (HTTr), high-throughput phenotypic profiling (HTPP) and a variety of associated computer modeling approaches predicting chemical mechanism of action, chemical exposure, use and potency. This work supports the EPA Administrator's Directive to reduce mammal studies by 30 percent by 2025 and eliminate all mammal studies by 2035. (https://www.epa.gov/research/efforts-reduce-animal-testing-epa)

Unilever also has a long history of developing and using non-animal methods to evaluate the safety of chemicals in their products, complies with legislation that bans the use of animal testing of cosmetic ingredients and would conduct, commission or pay for animal testing only when required by a government agency. Unilever and CCTE have each developed their own NAMs and have been jointly evaluating and using some common NAMs through a CRADA that has run from 2015-2020. The learnings from this prior CRADA form the foundation for the new proposed efforts to show how new methods and approaches can be brought together to make a safety decision that assures the protection of consumers, workers and the environment rather than predicting the incidence of apical endpoints in animals. There will be several interlinked goals, but all will make use of a large data set to be jointly developed. An additional aspect of this CRADA will be the evaluation of the common chemical set using available computer models developed by both the EPA Duluth Lab and by Unilever to address how (and to what extent) we can use data, derived ostensibly for the purposes of a human health risk assessment, to inform an environmental risk assessment, by considering target and pathway homology.

The Key Outputs:

1. Develop a comprehensive NAMs data set (see below table) across multiple labs and technologies on a minimum of 40 chemicals (the "project chemicals") to be used to evaluate The Next Generation Blueprint of Computational Toxicology at the U.S. Environmental Protection Agency (https://academic.oup.com/toxsci/article/169/2/317/5369737) and the Unilever NGRA Toolbox.
2. Show how the EPA Blueprint of using HTTr and HTPP broad coverage tools, in combination with computational methods, can be complemented by other broad coverage tools such as the Unilever Cell Stress Panel and Pharmacological Target Safety Screen to make an NGRA decision or to direct higher-tier targeted NAMs testing towards an NGRA decision.
3. Use portions of this data set to develop prototype risk assessment dossiers (including read across) to present externally at conferences and across the scientific community, in order to start making the case for regulatory acceptance of specific assays or technologies that support the Blueprint and Toolbox; i.e. develop and publish a set of recommendations for a NAM battery for evaluating the safety of new chemicals.
4. Explore the potential use of human safety data to inform on environmental risk assessment alongside with the application of cross species extrapolation computational tools (e.g. SeqAPASS)

For the purpose of this SOW, NAMs will mean any experimental or computational method or model that does not use whole animals. Examples are in vitro assays, QSAR models, toxicokinetics models, and models of species similarity.

Generic Tasks:

1. Select 40 chemicals and their exposure or 'risk' category (see Chemical Selection)
2. Order chemicals and deliver to all labs
3. Select HTTr and HTPP cell lines (12 each – as far as is practically possible, the same lines for the two technologies). Of these 10 would be from human tissues and 2 from fish cell lines. The human cell lines would be selected from the set already onboarded in the EPA Center, and must be compatible with the HTTr and HTPP assays as currently configured, which would rule out spheroids or suspension cultures. For the fish cell lines to be used, they would have to be shown to culture well and to be compatible with the HTPP cell painting assay.
4. Run the assay set – the initial set of assays will include the Unilever Toolbox set and assays being developed at EPA
5. Analyze the results of the battery and make recommendations on next steps
6. Explore the utility of human derived data for inferring toxicological effects in environmental relevant species.
7. Hold annual face-to-face meetings of the Unilever and EPA research teams and disseminate the science externally.
8. EPA issues annual progress reports.

Division of NAMs:

UNILEVER	EPA
HTTr in HepG2, MCF7 and HepaRG	HTTr in 10 human cell types + 2 fish lines
Cell Stress panel in HepG2 and additional cell types as appropriate	HTPP in 10 human cell types + 2 fish lines
Safety Screen panel	Add metabolic capacity to one or more HTTr or HTPP cell system
In silico (QSAR and MIE Atlas) battery	Assays for HTTK (fraction unbound, intrinsic hepatic clearance, absorption blood:plasma ratio)
Cytotoxicity panel	*In vitro* disposition (i.e. true *in vitro* dose over time)
Metabolite determination in selected cases	Metabolite determination in selected cases
Additional Unilever panels if they become available	Additional EPA devtox, neurotox and cardiotox panels if they become available
Unilever SEAC Genes to Pathways (G2P) tool	EPA SeqAPASS analysis

Resources will be set aside to add new assays as they become available. New chemicals will also be added to evaluate certain technologies/assays more deeply. This may include temporal and repeat dosing to reduce uncertainty in the risk assessment decision.

Analysis Approaches:
Each party will use their own analysis and modeling approaches (concentration-response, PK, biological pathways/network, risk assessment, POD determination, uncertainty quantification), but will comprehensively share methodology and results. Every effort possible will be taken to harmonize these approaches as the CRADA develops, so that a ONE TEAM approach is the ultimate output. As part of the approaches, key "gold standard" datasets where known dose response information can be inferred should be developed and utilized to strengthen comparisons of analytical approaches. Any modelling code and associated documentation generated by either party, as part of this CRADA, will be shared.

Defined Tasks:

Task 1: Selection of Chemicals
The initial chemical set should be a minimum of 40 chemicals, overlapping where possible with the Unilever 2020+ plans for evaluating the Systemic Toolbox v1. Traits of the chemical set will be:

1. Half 'benign' and half 'toxic' (at a given exposure scenario), where all the chemicals should have existing *in vivo* data or human safety data (e.g. history of safe use or known human toxicity) to establish their risk category.

2. Chemicals should be of interest to both Unilever and EPA
3. A small limited number of chemicals can be repeats of those already tested or already in existing data; new testing will help measure reproducibility of the repeated assays
4. Potentially a few close pairs should be included to test read-across methods
5. Toxic chemicals should include some with specific MOA and some with more general systemic toxicity
6. EPA will provide input in chemical selection and will work with Unilever to determine chemical sourcing to ensure availability to all EPA commissioned laboratories for testing.
7. During selection of the chemical set, consideration should be made to better facilitate cross-species extrapolation approaches.

Center Responsibilities: EPA will advise on chemical selection, purchase, and distribute.

Cooperator Responsibilities: Unilever will take the lead in defining the 40 chemicals with input from EPA.

Deliverables:

- Year 1: (1) Select 40 chemicals; (2) source chemical samples and deliver to labs
- Year 2: No actions
- Year 3: No actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $25K to purchase and distribute chemicals, 0.2FTE to select chemicals
- EPA: 0.13 FTE to manage chemical procurement and select chemicals

Task 2: Selection of Cell lines for HTTr and HTPP

The selection of the cell lines will be informed by the previous Unilever/EPA CRADA studies along with additional technical insights from both teams which will enable experimental comparisons and aid risk assessment dossier generation. In addition, 1 or 2 environmentally relevant cell lines (e.g. fish) will be included and an appropriate custom HTTr panel based on the whole transcriptome of the selected environmental species will need to be sourced/developed.

Center Responsibilities: EPA will take the lead in determining data driven biological space coverage and inform on pragmatic requirements to enhance similarities across HTPP and HTTr.

Cooperator Responsibilities: Unilever will take the lead to assess results of Unilever compounds across the various cell lines for input into final cell line selection and will also inform on suggestions that will strengthen risk assessment prototype dossiers.

Deliverables:

- Year 1: Select first 6 cell lines
- Year 2: Select second 6 cell lines based on results of first 6. Fish cell lines will be used in year 2.
- Year 3: no actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: 0.5 FTE
- EPA: 0.51 FTE

Task 3: Conduct of the Cell Stress panel, Safety Screen target panel, In Silico Battery and the Cytotoxicity Panel (the NGRA Toolbox)

Cell stress panel data to be generated for 40+ chemicals, consisting of 36 biomarkers representing 9 stress pathways or cell heath endpoints, measured predominantly using high content imaging. Extended safety screen target panel to consisting of 24 GPCRs, 8 ion channels, 7 enzymes, 3 transporters and 18 nuclear receptors.

Center Responsibilities: None

Cooperator Responsibilities: Unilever will conduct in-use scenario relevant exposure models for the series of 40+ chemicals being studied. In addition, Unilever will analyze the same chemicals through their current systemic tox toolbox v1 (including as a minimum computations screens, cytotoxicity, cell stress panel, target screens) and make the results available for mutual sharing.

Deliverables:

- Year 1: Carry out first phase of screening on project chemicals
- Year 2: Finalize screening of project chemicals
- Year 3: No actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: 0.5 FTE
- EPA: No contribution

Task 4: Addition of metabolic capacity to one cell line for use in HTTr and HTPP

Metabolic competency is key to ensuring that any *in vitro* effects observed are representative of those which would be manifested *in vivo*. As such steps will be taken to ensure that metabolism has been considered and where appropriate integrated into all data generation approaches.

Center Responsibilities: EPA will develop a protocol to run HTTr and HTPP in one cell line in which metabolic activation has been added. This will use a variant of the current 384-well approaches developed by EPA.

Cooperator Responsibilities: Unilever will apply their Metabolism Framework to provide predictive and (where relevant) experimental insights into the metabolism of each of the 40+ chemicals.

Deliverables:

- Year 1: Select cell line to have metabolic competency added
- Year 2: Run project chemicals in this cell line both with and without metabolic competency
- Year 3: No actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $10K for reagents at EPA and technician support
- EPA: 0.23 FTE to develop metabolically competent system

Task 5: Run HTTr in 12 cell lines
EPA will perform cell culture and dosing for 40 chemicals. These include both the 10 human cell lines and 2 fish cell lines. Cell lysate will be shipped to BioSpyder to perform further processing and sequencing. EPA staff will process the data to provide results as normalized counts and log2 fold changes. Data (including raw data files) will then be shared with Unilever.

Center Responsibilities: EPA will generate data using a combination of in-house laboratories and contractors

Cooperator Responsibilities: Unilever will conduct HTTr analysis on the same 40+ chemicals in HepG2, MCF7 and HepaRG. Raw data, normalized counts and log2 fold changes will be shared with EPA.

Deliverables:
- Year 1: (1) Dose cells with project chemicals for first 6 cell lines; (2) have sequencing performed for these 6 cell lines; (3) perform all computational processing for these 6 cell lines
- Year 2: (1) Dose cells with project chemicals for second 6 cell lines; (2) have sequencing performed for these 6 cell lines; (3) perform all computational processing for these 6 cell lines
- Year 3: No actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):
- Unilever: $1091K for sequencing and $160K for technician support
- EPA: 0.21 FTE

Task 6: Run HTPP in 12 cell lines
EPA will perform cell culture, dosing, and cell painting. These include both the 10 human cell lines and 2 fish cell lines. Data will be processed to produce concentration-response profiles at multiple levels, and this data will be provided to Unilever.

Center Responsibilities: All Center work and data analysis will be performed by EPA

Cooperator Responsibilities: Unilever will analyze data using their own point of departure modelling approaches and share results

Deliverables:
- Year 1: (1) Dose cells with project chemicals for first 6 cell lines; (2) perform all computational processing for these 6 cell lines
- Year 2: (1) Dose cells with project chemicals for second 6 cell lines; (2) perform all computational processing for these 6 cell lines
- Year 3: No actions

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $42K for reagents
- EPA: 0.21 FTE

Task 7: Run assays required for toxicokinetics (TK)

High throughput toxicokinetic modeling requires at a minimum the measurement of fraction unbound in plasma (fup) and intrinsic hepatic clearance (Clint) for each chemical. For chemicals in the CRADA set that do not have this information, EPA will attempt to develop analytical chemistry methods (a prerequisite for these measurements). For chemicals where analytical methods are successful, measurements of fup and Clint will be performed. The resulting data will be incorporated into the EPA HTTK R package to allow toxicokinetics modeling. Additional in vitro measurements (for example, membrane permeability and blood: plasma chemical concentration ratio) are currently being investigated to refine toxicokinetic modeling. If suitable assays are available and refinements of predictions are desired these may also be conducted. The Center tasks (analytical chemistry method development, and in vitro measurements) may be carried out at EPA labs or may be contracted out. All results will be provided to Unilever.

Center Responsibilities: EPA will manage the production of the TK data

Cooperator Responsibilities: None

Deliverables:

- Year 1: (1) survey existing toxicokinetics (TK) data for project chemicals to see which have existing data; (2) send remaining chemicals to analytical labs to develop analytical methods
- Year 2: (1) Carry out TK Center measurements for all chemicals with acceptable analytic methods; (2) process data into the EPA HTTK package; (3) run QSAR model to predict TK parameters for chemicals without acceptable experimental data
- Year 3: (1) Identify and make machine-readable any in vivo TK data for the 40 chemicals in the scientific literature. Perform a statistical evaluation of the in vitro predictions using the available data.

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $264K for contract work to run HTTK-related assays
- EPA: 0.33 FTE

Task 8: Run in vitro disposition measurements

This task will use analytic methods to determine how much of a chemical partitions into the different components of the in vitro system including cells, cell culture vessels, and media.

Center Responsibilities: The Tox21 partners have a collaborative project to assess the in vitro disposition of chemicals. Using the methods worked out in the Tox21 cross-partner project, the in vitro disposition will be carried out on 40 chemicals in select cell lines (no more than 2). This work will be performed in the EPA laboratories in CCTE.

Cooperator Responsibilities: Unilever will apply their True Dose Framework to provide predictive

and (where relevant) experimental insights into the partitioning of each of the 40+ chemicals within the *in vitro* NAMs being used.

Deliverables:

- Year 1: (1) Develop protocol to determine in vitro disposition; (2) perform proof-of-principle experiments to determine feasibility of the approach
- Year 2: (1) Carry out preliminary analyses on first batch of data on the project chemicals; (2) Develop joint publication plan; (3) make public presentations at one or more meetings.
- Year 3: (1) Carry out analyses of complete dataset; (2) develop one or more manuscripts based on the data sets; (3) Make public presentations at one or more meetings.

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $45K for instrument costs, analytical supplies, and technician support
- EPA: 0.83 FTE

Task 9: Metabolite determination

This task will use non-targeted analytic methods to detect and identify metabolites of a selected set of the project chemicals.

Center Responsibilities: EPA labs will incubate individual chemicals with rodent and human hepatocytes and analyze these samples for hepatic clearance and metabolite production using non-targeted analysis.

Cooperator Responsibilities: Unilever will provide their expertise to consult on the method development for metabolite determination.

Deliverables:

- Year 1: (1) Develop protocol to predict possible metabolites; (2) perform proof-of-principle experiments to determine feasibility of the approach
- Year 2: (1) Carry out preliminary analyses on first batch of data on the project chemicals; (2) Develop joint publication plan; (3) make public presentations at one or more meetings.
- Year 3: (1) Carry out analyses of complete dataset; (2) develop one or more manuscripts based on the data sets; (3) Make public presentations at one or more meetings.

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $165K for analytical supplies, machine support and technician support
- EPA: 0.73 FTE

Task 10: Analysis of combined human- health focused data set

NAMs data generated by both parties will be evaluated and modelled with the aim of being able to derive exposure-based safety risk assessments. Data will be analyzed both as individual sets and as combined multi-variate datasets with the aim of providing a weight of evidence approach to understanding perturbed pathways and defining margins of safety towards safety decisions. Raw data, derived data and modelling approaches will be shared.

Center Responsibilities: EPA will use methods within their Alternatives Roadmap to develop

decision making approaches using the data being generated on the project chemicals.

Cooperator Responsibilities: Unilever will use their NGRA framework and associated decision-making tools to develop decision making approaches and communications based on the use of NAMs data developed within this CRADA

Deliverables:

- Year 1: (1) Develop protocols for sharing data including formats and methods for data transfer; (2) develop general analysis strategies to be carried out separately and jointly; (3) Share preexisting data (e.g. on HTS, HTTK, chemical properties, etc.)
- Year 2: (1) Carry out preliminary analyses on first batch of data on the project chemicals; (2) Develop joint publication plan; (3) make public presentations at one or more meetings.
- Year 3: (1) Carry out analyses of complete dataset; (2) develop one or more manuscripts based on the data sets; (3) Make public presentations at one or more meetings.

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: 1.5 FTE
- EPA: 1.11 FTE

Task 11: Cross-species extrapolation

Understand the conservation and relevance of targets and toxicity pathways, identified through HTTP and HTTr screening using human and fish cell lines, across environmentally relevant species to inform on the environmental susceptibility space and ultimately directing Environmental Risk Assessment (ERA). This will be achieved using a suite of bioinformatics tools encompassing genomics, phylogenetics and PBK approaches.

Center Responsibilities: The EPA will analyze HTTr and HTTP data generated from 10 human cell lines and 2 fish cell lines and provide inhouse informatics approaches (e.g. SeqAPASS) to identify target homology between human and other environmentally relevant (notably fish) species.

Cooperator Responsibilities: Unilever will provide inhouse informatics approaches (e.g. Genes 2 Pathways (G2P) tool) to identify pathway homology between human cell lines and other environmentally relevant (notable fish) species. Unilever will also estimate internal exposure in fish using TK/ PBPK models.

Monetary and In-kind Expenditure Estimates (cumulative over 3 years):

- Unilever: $255K to support Postdoc at EPA; 0.4 FTE

EPA: 0.33 FTE

Deliverables

- Year 1: (1) Comparison of available in vitro / transcriptomics data with available *in vivo* endpoint data to assess if they are protective. (2) A conceptual integration of output from SeqAPASS and G2P tools.
- Year 2: (1) Defined PODs derived from HTTr and HTPP data (human cell lines) and their relevance to environmentally relevant (notably fish) species. (2) Develop case examples

demonstrating utility of SeqAPASS and G2P data integration for extrapolating HTTr and HTPP results beyond the model organisms in the assays. Compare results from bioinformatic tools to results collected comparing fish and human.

- Year 3: (1) Benchmarked PODs derived from human cell with those in fish cell lines (2) Margins of Safety (MoS) derived for fish using PODs, qIVIVE and PBPK modelling. Develop and submit manuscript describing results generated from the conceptual integration of results from SeqAPASS and G2P tools with case examples demonstrating the utility of these data for integration in risk assessment.

In-kind Expenditures

Unilever will contribute 3.10 FTE in-kind / over the three-year period of this agreement
Estimated total in-kind personnel resource from Unilever, equivalent contributions: $393,700

EPA will contribute 4.62 FTE in-kind / over the three-year period of this agreement
Estimated total in-kind personnel resource from EPA, equivalent contributions: $749,330.

Summary of Center Resources
Center resources: The Center will carry out experimental work on HTTr, HTPP, toxicokinetics and in vitro disposition. It will further carry out computational data processing and modeling using data from the project chemicals. EPA facilities will be used for appropriate experimental work. EPA will manage external contracts as needed, for instance in processing and sequencing of HTTr samples, and maintenance and development of SeqAPASS.

Cooperator resources: Provision of technical assistance via scientist to scientist discussions on a regular basis by video-conferencing/TC and visits to SEAC and the EPA, data analyses and supporting research, e.g. through the Unilever in-use scenario relevant exposure models and toolbox assay set data generation (including use of facilities, personnel and supplies), as needed.