

MATERIALS COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT (MCRADA)

This Materials Cooperative Research and Development Agreement (“MCRADA” or “Agreement”) is entered into by and between Syngenta Crop Protection, LLC, a Delaware Corporation which has its principal place of business at 410 Swing Road S, Greensboro, NC 27409 (“the Collaborator”), and the Center for Computational Toxicology and Exposure (“CCTE” or “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. The Collaborator agrees to transfer to CCTE the following Research Material:

Acibenzolar-S-methyl and carboxylic acid metabolite of acibenzolar-S-methyl (benzo[1,2,3]thiadiazole-7-carboxylic acid)

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 DURC Internal Review Entity (IRE) has determined that this research does not meet the DURC definition and that no additional review and oversight under the *USG Policy for Institutional Oversight of DURC* are required. The Principal Investigator (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 PI feels that the research may be DURC.
4. No Transfer. CCTE’s investigator agrees to retain control over the Research Material transferred to them and further agrees not to transfer the Research Material to other people not under their direct supervision without advance written approval of the provider of said Research Material. CCTE shall not use the Research Material received under this Agreement for any other purpose other than the research as described in Appendix A (“RESEARCH”). The Collaborator reserves the right to distribute their own Research Material to others and to use it for their own purposes.
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 submitted 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 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 Collaborator, 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. CCTE agrees to use its best efforts to protect the information designated as Proprietary Information from unauthorized disclosure for a period of three (3) years from the date of the disclosure. 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 Material is provided as a service to the research community. IT IS 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 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; however, no indemnification is provided or intended.
7. Intellectual Property. CCTE and the Collaborator believe that no Subject Inventions or Computer Software will be created during the work specified in this Agreement. Should it appear that any activity of this Agreement might involve the creation of Subject Inventions or Computer Software, CCTE and the Collaborator will negotiate a standard CRADA in good faith. The standard CRADA will assign responsibilities for obtaining patents or other intellectual property rights pertaining to the Subject Inventions or Computer Software and will provide for appropriate allocation of any patent or intellectual property rights resulting from those Subject Inventions or Computer Software. For the purposes of this section, "Subject Invention" means any invention, conceived or first actually reduced to practice in the performance of this Agreement, and "Computer Software" means computer software, computer programs, computer data

bases, and documentation thereof developed in whole or in part under this Agreement.

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 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. Nothing in this Agreement will prevent the Collaborator from pursuing such additional administrative remedies as may be available and, after exhaustion of such administrative remedies, pursuing available judicial remedies.
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:

Alice Ng
Head CP Human Safety NA
410 Swing Road S, Greensboro, NC 27409 USA
sheung.ng@syngenta.com
1-845 558 1238

With a copy to:

Brianna Jackson
NA Human Safety Project Expert
410 Swing Road S, Greensboro, NC 27409 USA
brianna.jackson@syngenta.com

(b) If to CCTE:

EPA- Syngenta Crop Protection, LLC- MCRADA # 1554-24

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
EPA FTTA Program Coordinator
graham.kathleen@epa.gov
(303) 312-6137
ftta@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, CCTE does not directly or indirectly endorse 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.
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

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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 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 12 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:  _____ Date _____


For the Collaborator:

By:  _____ Date: 


APPENDIX A

RESEARCH PLAN

EPA will test acibenzolar-S-methyl and its carboxylic acid metabolite in its developmental neurotoxicology new approach methodologies (DNT-NAMs). Specifically, the compound will be tested in the following assays which are listed in the Organization for Economic Cooperation and Development (OECD) initial guidance document on in vitro approaches for developmental neurotoxicity:

Proliferation/apoptosis/viability in hNP1 cells

Neurite outgrowth in human inducible pluripotent stem cell derived neurons (Igluta cells from Fuji Cellular Dynamics)

Neurite outgrowth in rat cortical cells

Neurite Maturation and Synaptogenesis in rat cortical cells

Network Formation in rat cortical cells

The material will be tested in triplicate in each assay at a concentration range decreasing in half log units in each assay with the highest concentration being tested of 30 for acibenzolar-S-methyl and 300 uM for its carboxylic acid metabolite. Each assay incorporates viability assessments.

Data from the EPA assays as well as data from other OECD approved assays (UKN and IUF) will be pipelined through EPA's ToxCast Pipeline. Data will be interpreted collectively to build a case-study of a compound that has a guideline DNT and data from DNT NAMs assays for both the parent and metabolite. It will provide an example of how DNT NAM data can inform the interpretation of data from guideline DNT studies to improve the scientific rigor of conclusions from those studies. All parties agree to make the data available to the public through EPA's ToxCast program.