MATERIALS TRANSFER AGREEMENT

Provider:
U.S. Environmental Protection Agency (EPA)
Office of Research and Development (ORD)
National Center for Computational Toxicology (NCCT)

Recipient:
Cosmetics Europe
Avenue Herrmann-Debroux 40
1160 Brussels; Belgium

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

Chemicals and Materials

- ☐ A list identifying selected chemicals from the ToxCast chemical library to be tested by XXXXX.
- ☐ A copy of the current ToxCast chemical library, or subset, consisting of chemical samples prepared as solution in dimethyl sulfoxide at a concentration of 20 millimolar. Additional chemicals may be provided in the future concurrent with expansion of the ToxCast chemical library.
- ☐ Samples of nanomaterials and characterization data on said materials.

Data and Summary Information

- ☐ In vitro assay data derived from the ToxCast Program. This data is derived from chemicals analyzed using a variety of high throughput assay techniques. Below this is referred to as the "ToxCast Data."
- ☐ In vivo whole animal toxicology data summary data derived from the EPA Toxicology Reference Database (ToxRefDB). Below this is referred to as the "ToxRefDB Data."
- ☐ Summary descriptions of the individual data sets.
- ☐ Individual subsets of this data will be delivered to XXX after they have been prepared for use at EPA and cleared for release to XXXX.
- X *In vitro* toxicokinetic data and summary spreadsheet, including Caco2 membrane permeability, hepatocyte suspension clearance, and rapid equilibrium dialysis measurements of plasma protein binding.

1b. The Recipient agrees to transfer to the EPA Investigator named below the following Research Material:

- ☐ All data or data summaries resulting from chemical screening performed on the ToxCast chemical library.
- ☐ Results of any data analyses that include use of provided ToxCast or ToxRef data.
- ☐ Relevant data on these chemicals from non-public sources.
- ☐ Unique chemicals for the ToxCast chemical library and subsequent testing by EPA.
- X The outcome of these data once available. EPA agrees not to release these data until Recipient publishes or makes available to the public.

2. This Research Material may not be used in human subjects. The Research Material will be used only for research purposes by Recipient's investigator, for the research project described below, under suitable containment conditions. This Research Material will not be used for screening, production or sale, for which a commercialization license may be required. Recipient agrees to comply with all Federal rules and regulations applicable to the Research Project and the handling of the Research Material.

EPA ONLY: If the data or material that are being transferred constitute human subjects research, please visit the following intranet site to determine if your project needs review and approval by the HSRRO: http://intranet.ord.epa.gov/p2/hsr/human-subjects-review.

X There is no Human Subjects material being used in this research.

☐ Research Plan reviewed and approval by HSRRO: Name_____
Date__/__/_____

3. If the data or material that are being transferred involve life sciences research or more specifically, any of the select agents or toxins listed, and/or the definitions provided in EPA Order 1000.19 *Policy and Procedures for Managing Dual Use Research of Concern*, then Principal Investigators should consult EPA's Institutional Contact for Dual Use Research of Concern (ICDUR) at DURC@epa.gov before completing the following section. If not, then check the first box below.

X This research does not meet any of the definitions of Dual Use Research of Concern (DURC) and no additional review or oversight are required. The PI must report to the ICDUR any results or changes in the research that meet any of the definitions of DURC.

☐ This research meets one or more definitions of DURC and requires additional oversight under the *USG Policy for Institutional Oversight of DURC*. The parties to this Agreement are required to comply with EPA Order 1000.19, *Policy and Procedures for Managing Dual Use Research of Concern*.

For information about DURC and EPA Order 1000.19, please visit:
http://intranet.ord.epa.gov/homeland-security/dual-use-research-concern-durc-policies.

4. This Research Material will be used by Recipient's investigator and the internal TTC working group – a working group consisting of experts from various institutions - solely in connection with the following research project ("Research Project") described with specificity as follows:

> EPA will provide access to *in vitro* Caco2 membrane permeability data. The Threshold of Toxicological Concern (TTC) is an important risk assessment tool which establishes acceptable low-level exposure values to be applied to chemicals with limited toxicological data. One of the logical next steps in the continued evolution of TTC is to develop this concept further so that it is representative of internal exposures (TTC based on plasma concentration). An internal TTC (iTTC) would provide threshold values that could be utilized in exposure-based safety assessments. Cosmetics Europe has initiated a project that is working towards the development of iTTCs that can be used for the human safety assessment. The CaCo2 and other ADME data will be used in the PBPK modelling in this project.
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> The dermal route is an important contributor to chemical exposure for consumers and people in occupational settings. The NCCT has already developed a high throughput physiologically-based toxicokinetic (HT-PBTK) model to simulate oral exposure. However, NCCT is now developing a HT-PBTK model to simulate dermal exposure to chemicals. This model will allow for *in vitro-in vivo* extrapolation (IVIVE) of bioactivity data identified by high throughput screening exercises such as ToxCast.
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> EPA aims to be able to simulate dermal exposures for people in consumer and occupational settings rapidly using data obtained from *in vitro* assays. EPA will use Recipient's analysis response to develop the model. The development of the model will be addressed in a subsequent cooperative research agreement.

5. In all oral presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material unless requested otherwise. To the extent permitted by law, Recipient agrees to treat as confidential, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL" for a period of three (3) years from the date of its disclosure to recipient. The foregoing shall not apply to information that is or becomes publicly available or which is disclosed to Recipient without a confidentiality obligation. Any oral disclosures from Provider to Recipient, which Provider wishes to be treated as confidential shall be identified as being Confidential at the time of the disclosure and by written notice delivered to Recipient within thirty (30) days after the date of the oral disclosure. Recipient may publish or otherwise publicly disclose the results of the Research Project, but if Provider has given Confidential information to Recipient, such public disclosure may be made only after Provider has had thirty (30) days to review the proposed

disclosure to determine if it includes any Confidential information, to the extent such review period is permitted by law.

6. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipient's investigator therefore agrees to retain control over this Research Material and further agrees not to transfer the Research Material to other people not under his/her direct supervision without advance written approval of Provider, apart from the experts of the internal TTC working group. Provider reserves the right to distribute the Research Material to others and to use it for its own purposes. When the Research Project is completed, the Research Material will be returned to the Provider or disposed, if directed by Provider.

7. This Research Material is provided as a service to the research community. It is being supplied to Recipient with no warranties, express or implied, including any warranty of merchantability or fitness for a particular purpose. Provider makes no representations that the use of the Research Material will not infringe any patent or proprietary rights of third parties.

8. Recipient shall retain title to any patent or other intellectual property rights in inventions made by its employees in the course of the Research Project. However, if said inventions contain any portion of the Research Material, are derived from the Research Material, or could not have been produced but for the use of the Research Material, Recipient agrees to contact the Provider to determine what ownership interests, if any, the Provider may have, and, where applicable, to negotiate in good faith the terms of a commercial license. Inventorship for a patent application or a commercialized product based on said inventions shall be determined according to United States patent law.

9. When Provider is the EPA: Recipient agrees not to claim, infer, or imply endorsement by the Government of the United States of America (hereinafter referred to as "Government") of the Research Project, the institution or personnel conducting the Research Project, or any resulting product(s). Recipient agrees to hold the Government harmless and to indemnify the Government for all liabilities, demands, damages, expenses, and losses arising out of Recipient's use for any purpose of the Research Material.

10. When Recipient is the EPA: Provider will not be liable to EPA for any claims or damages arising from EPA's use of the Research Material.

11. The Provider shall have the right to terminate this Agreement at any time if Recipient breaches any of the terms of this Agreement. Upon termination, Recipient shall return to the Provider all unused portions of the Research Materials.

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

____ Yes – go to item A

_X___ No – skip to #13 (next clause)

Item A: The EPA laboratory must coordinate on matters related to Quality Assurance with their QA Specialist.

_____ If necessary, the Laboratory will develop/has developed a Quality Assurance Plan in coordination with the Quality Assurance Specialist.

_X____ No QA requirements are needed.

13. All notices pertaining to or required by this Agreement shall be in writing and shall be signed by an authorized representative and shall be delivered by hand (including private courier mail service) or sent by certified mail, return receipt requested, with postage prepaid, addressed as follows:

Provider's Contact Information:
Russell Thomas
U.S. EPA National Center for Computational Toxicology (NCCT)
109 T.W. Alexander (MD-D-143-02)
Research Triangle Park, NC 27711
919-541-5776
thomas.russell@epa.gov

With a copy to:
Sandra Roberts
U.S. EPA National Center for Computational Toxicology (NCCT)
109 T.W. Alexander (MD-D-143-02)
Research Triangle Park, NC 27711
919-541-3850
roberts.sandra@epa.gov

For commercial courier address use:
4930 Old Page Road
Durham, NC 27703

AND

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

Recipient's Contact Information:

John Chave
Director General
Avenue Herrmann-Debroux 40
1160 Brussels; Belgium
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jchave@cosmeticseurope.eu

With a copy to:

Martina Klaric
Research Project Manager
Avenue Herrmann-Debroux 40
1160 Brussels; Belgium
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mklaric@cosmeticseurope.eu

14. Paragraphs 2, 7, 9, and 10 shall survive termination.

15. This Agreement shall be construed in accordance with law as applied by the Federal courts in the District of Columbia.

16. The undersigned Provider and Recipient expressly certify and affirm that the contents of any statements made herein are truthful and accurate.

17. This agreement shall enter into force as of the date of the last signature of the parties and shall remain in effect for one year from said date.

Any false or misleading statements made, presented, or submitted to the Government, including any material omissions, under this Agreement and during the course of negotiation of this Agreement are subject to all applicable civil and criminal statutes including 31 U.S.C. §§ 3801-3812 (civil liability), 18 U.S.C. §§ 1001 (criminal liability), and 31 U.S.C. §§ 3729-33 (False Claims Act).