Instruction Sheet for Tie2ERT2Cre transgenic mouse Material Transfer Agreement (MTA) for Academic Centers (Non-profit)

In order to make our process for sending this popular material more efficient, DKFZ has created a non-negotiable, simple Material Transfer Agreement that is ready for an institution and its scientist to sign. The Material will be made available by a third party **(European Mouse Mutant Archive (EMMA))**. We have used standard terms that we find most institutions can agree to.

In order to receive the Tie2ERT2Cre material, please follow these instructions:

1. Complete the following information:

a) In the opening paragraph, fill in the institute’s legal name, place of business, and the recipient scientist’s name in the appropriate places.

b) In Section II please check the paragraph regarding genetically modified organism and have it signed by the legal representative of your institution.

c) On the final page, please have the Recipient Scientist and the appropriate legal representative of the institution sign and date the agreement.

2. Send the MTA to:

 Innovation Managament T010

 Deutsches Krebsforschungszentrum

 Im Neuenheimer Feld 280

 69120 Heidelberg

 Germany

If your institution does not require hardcopies, please send a PDF to: mta@dkfz.de

When sending us the MTA, please advise who at the institution should receive the fully signed copy of the MTA once completed by DKFZ

3. We will process the MTA as soon as possible and return one fully executed MTA to the institution receiving the material. Once the MTA is fully executed, you can request the mice from the **European Mouse Mutant Archive (EMMA)**, Campus A. Buzzati-Traverso, Via E. Ramarini, 32, I-00016 Monterotondo Scalo, Rome, Italy, Fax: +39-0690091260

Please provide EMMA with a copy of the fully executed MTA when ordering the mice.

If you have any questions, please send an e-mail to mta@dkfz.de.**Transfer of Biological Material**

Deutsches Krebsforschungszentrum, Stiftung des öffentlichen Rechts (German Cancer Research Center) located at Im Neuenheimer Feld 280, D-69120 Heidelberg, Germany ("DKFZ") agrees to provide  (name of institution) located at

("RECIPIENT"; address) with certain MATERIAL for use in the laboratory of

 (“RECIPIENT SCIENTIST”; name) for the purpose of conducting scientific work in the topic of  (specification of experiments) under the following conditions:

At the request of RECIPIENT and at RECIPIENT's own risk and responsibility, the MATERIAL will be made available to RECIPIENT by a third party **(European Mouse Mutant Archive (“EMMA”))**, Campus A. Buzzati-Traverso, Via E. Ramarini, 32,

I-00016 Monterotondo Scalo, Rome, Italy). DKFZ retains ownership of the MATERIAL.

**I.**

Definitions:

1. MATERIAL: ORIGINAL MATERIAL; PROGENY; and UNMODIFIED DERIVATIVES. The MATERIAL shall not include: (a) MODIFICATIONS, or (b) other substances created by the RECIPIENT through the use of the MATERIAL which are not MODIFICATIONS, PROGENY, or UNMODIFIED DERIVATIVES.
2. PROGENY: Unmodified descendant from the MATERIAL, such as virus from virus, cell from cell, or organism from organism.
3. UNMODIFIED DERIVATIVES: Substances created by the RECIPIENT which constitute an unmodified functional subunit or product expressed by the ORIGINAL MATERIAL.
4. MODIFICATIONS: Substances created by the RECIPIENT which contain/incorporate the MATERIAL.

**II.**

**Please check and sign the following:**

🞏 Material is a genetically modified organism classified in risk group 1

 RECIPIENT confirms by the signature below that it is authorised and has
 adequate facilities which comply with all laws and regulations applicable in
 RECIPIENT’s country to work with genetically modified organisms

 Authorized Official of Recipient

 (Person authorized to bind RECIPIENT legally by his/her signature)

 Name:

 Position:

 Signature: ……………………………………………………..

The ORIGINAL MATERIAL created by Dr. Bernd Arnold that is covered by this Agreement is:

the **Tie2ERT2Cre transgenic mouse**, which contains the Tie2 promoter provided by Dr. Tom Sato, a faculty member at The University of Texas Southwestern Medical Center at Dallas (“UT Southwestern”). It contains further the recombinase Cre-ERT2 provided by Prof. Dr. Pierre Chambon of the GIE-CERBM, Institut de Génétique et de Biologie Moléculaire et Cellulaire, 67404 Illkirch Cedex, France (“GIE-CERBM“).

The MATERIAL listed above is considered proprietary to DKFZ. The Tie2 promoter is considered proprietary to UT Southwestern and Beth Israel Deaconess Medical Center (“BIDMC”). The recombinase Cre-ERT2 is considered proprietary to GIE-CERBM. The GIE-CERBM has designed the Cre-ERT2 construct and has been granted a US patent that covers the use of Cre-ERT2 (Patent no. 7,112,715 entitled: "Transgenic mouse for targeted recombination mediated by modified Cre-ER")

**III.**

The MATERIAL is to be used solely for teaching and academic research purposes and will not be used in human subjects, in clinical trials, or for diagnostic purposes involving human subjects without the written consent of DKFZ.

**IV.**

RECIPIENT shall not distribute or release the MATERIAL to any person other than laboratory personnel under RECIPIENT SCIENTIST’s direct supervision and shall ensure that no one will be allowed to take or send the MATERIAL to any other location unless written permission is obtained from DKFZ. DKFZ will control future distributions of the material. At the written request of DKFZ, RECIPIENT will cease to use MATERIAL and will return (at DKFZ’s option) all unused MATERIAL.

**V.**

DKFZ retains ownership of the MATERIAL, including any MATERIAL contained or incorporated in MODIFICATIONS. The UT Southwestern and Beth Israel Deaconess Medical Center (“BIDMC”) retain ownership of the Tie2 promoter. GIE-CERBM retains ownership of the recombinase Cre-ERT2 .

RECIPIENT retains ownership of: (a) MODIFICATIONS (except that DKFZ retains ownership rights to the MATERIAL included therein) , and (b) those substances created through the use of the MATERIAL or MODIFICATIONS, but which are not PROGENY, UNMODIFIED DERIVATIVES or MODIFICATIONS (i.e. do not contain the ORIGINAL MATERIAL, PROGENY, UNMODIFIED DERIVATIVES). If either (a) or (b) results from the collaborative efforts of DKFZ and RECIPIENT, joint ownership may be negotiated.

**VI.**

RECIPIENT shall have the right to distribute substances created by RECIPIENT through the use of the ORIGINAL MATERIAL, only if those substances are not PROGENY, UNMODIFIED DERIVATIVES or MODIFICATIONS.

Under a separate agreement at least as protective of DKFZ’s, GIE-CERBM, UT Southwestern's and BIDMC's rights as this Agreement, RECIPIENT may distribute MODIFICATIONS to non-profit organizations for research and teaching purposes only.

Without written consent of DKFZ, GIE-CERBM and UT Southwestern, RECIPIENT may not provide MODIFICATIONS for commercial purposes. It is recognized by RECIPIENT that such commercial purposes may require a commercial license from DKFZ, GIE-CERBM and UT Southwestern and that DKFZ, GIE-CERBM and UT Southwestern have no obligation to grant a commercial license to its ownership interest in the MATERIAL incorporated in the MODIFICATIONS.

RECIPIENT agrees that nothing in this Agreement shall be deemed to grant either any rights under any DKFZ patents nor any rights to use the MATERIAL nor any products or processes involving the MATERIAL for profit-making or commercial purposes. The MATERIAL will not be used in research that is subject to consulting or licensing obligations to another corporation, company, or business entity unless written permission is obtained from DKFZ, GIE-CERBM and UT Southwestern.

**VII.**

RECIPIENT shall periodically inform DKFZ of research results related to the MATERIAL and will provide DKFZ with a copy of any manuscripts describing the results of such research at the time the manuscript is submitted for publication. RECIPIENT shall mention DKFZ by name in any publication or the responsible DKFZ member as co-authors or in any other appropriate way.

**VIII.**

THE MATERIAL IS EXPERIMENTAL IN NATURE AND IS PROVIDED WITHOUT WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OR ANY OTHER WARRANTY, EXPRESS OR IMPLIED. DKFZ MAKES NO REPRESENTATION OR WARRANTY THAT THE MANUFACTURE, SALE, TRANSFER OR USE OF THE MATERIAL WILL NOT INFRINGE ANY PATENT OR PROPRIETARY RIGHT OF OTHERS.

**IX.**

MATERIAL as used herein and any cell line or progeny containing lox DNA or cre DNA derived directly or indirectly there from is covered by the claims of U.S. patent number 4,959,317, which has been assigned by DuPont Pharmaceuticals Company to Bristol-Myers Squibb Company (BMS).

If RECIPIENT has a license from DuPont (BMS), RECIPIENT may use the MATERIAL subject to the terms of that license. Alternatively, RECIPIENT shall be subject to paragraphs a), b) and c) below.

1. RECIPIENT may use the MATERIAL solely for its internal non-commercial biomedical research purposes, *provided however,* that such research purposes specifically excludes
2. use of cre DNA and/or lox DNA in higher plants or agricultural applications,
3. use of cre DNA and/or lox DNA in the alteration of mouse embryonic stem cells or other pluripotent mouse cells for the purpose of preparing a library of such mouse embryonic stem cells or other pluripotent mouse cells containing cre and/or lox DNA, and
4. use of any material containing cre DNA and/or lox DNA which is encompassed by U.S. patent number 4,959,317 for any commercial purpose or for the benefit of any for-profit institution. RECIPIENT shall not use the MATERIAL in the development, manufacture, use, lease, sale (or other transfer for consideration) or importation of any product for sale (or lease or other transfer of a product for consideration) wherein the manufacture use, sale or importation of such product would infringe U.S. patent number 4,959,317, including but not limited to wherein the product is manufactured using a composition or method whichwould infringe U.S. patent number 4,959,317. RECIPIENT shall not use the MATERIAL to generate scientific data or information that is conveyed to a third party for consideration, except as may be permitted under a written agreement between the non-profit institution and BMS.
5. The MATERIAL, and any PROGENY or DERIVATIVES containing cre DNA and/or lox DNA derived directly or indirectly there from, may not be transferred by the RECIPIENT to any third parties, except as may be permitted under a written agreement between the non-profit institution and BMS.
6. With respect to any questions regarding license rights under US patent No: 4,959,317, RECIPIENT should contact: Technology Group Bristol-Myers Squibb Company, Experimental Station -E 353 /224, Wilmington, Delaware 19880 and with a copy of all notices to Vice President and senior Counsel, Pharmaceutical Research, Institute and Business Development, PO BOX 4000, Princeton, New Jersey 08543 - 4000.

**X.**

DKFZ has a non-exclusive license from Cellectis, the exclusive licensee, to Institut Pasteur patent No. FR 2646438 and corresponding patent applications and patents. If MATERIAL is covered by such patents, RECIPIENT is not allowed to transfer any MATERIAL to third parties.

**XI.**

RECIPIENT shall notify DKFZ, GIE-CERBM and UT Southwestern promptly in writing of any invention, improvement, modification, discovery, or development (each, an "Invention") of MATERIAL or associated know how and data conceived or reduced to practice in the course of the RECIPIENT’s research with MATERIAL or associated know how and data. In the patent applications DKFZ, GIE-CERBM and UT Southwestern, respectively their employees, shall be mentioned as co-inventors according to their contribution to the invention, if appropriate under statutory provisions. If patents applications are filed in the United States, parties agree to abide by United States patent law.

RECIPIENT hereby grants DKFZ, GIE-CERBM, UT Southwestern and BIDMC a royalty-free, worldwide, non-exclusive license for their internal research purposes under any technology, any patent thereon and any material resulting from the use of the MATERIAL by RECIPIENT. If RECIPIENT commercially evaluates the research results, the parties shall start good faith negotiations leading to a sufficient participation of DKFZ, GIE-CERBM, UT Southwestern and BIDMC in RECIPIENT’s benefits.

**XII.**

In no event shall DKFZ, GIE-CERBM, UT Southwestern and BIDMC be liable for any use by RECIPIENT of the MATERIAL or any loss, claim, damage or liability, of whatsoever kind or nature, which may arise from or in connection with this Agreement or the use, handling or storage of the MATERIAL by RECIPIENT.

**XIII.**

RECIPIENT agrees to comply with all applicable laws, rules and regulations relating to the care, welfare, handling, breeding, storage, transfer and disposal of the MATERIAL, including all laws relating to shipment to and from (and which will be made F.O.B.) DKFZ, Heidelberg, Germany. To the extent permitted by law, RECIPIENT agrees to waive all claims against DKFZ, GIE-CERBM, UT Southwestern and BIDMC and to indemnify, defend and hold harmless DKFZ, its employees and agents, The University of Texas System, UT Southwestern, their Regents, officers, agents and employees, BIDMC and GIE-CERBM from and against all claims, damages and liability that may be asserted by third parties arising out of the use, care, handling, disposal, transfer, breeding and shipment of the MATERIAL, unless such claims, damages and liability are due to the gross negligence or willful misconduct of DKFZ, UT Southwestern, BIDMC or GIE-CERBM.

**XIV.**

Should any provision of this agreement be invalid or unenforceable or should the contract contain an omission, the remaining provisions shall be valid. In the place of an invalid provision, a valid provision is presumed to be agreed upon by the parties, which comes economically closest to the invalid provision. The same shall apply in the case of an omission. This wording contains the entire agreement between the parties; any changes of the agreement have to be made in writing.

Signatures on next page

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| Date: .......................................... |  | Date:................................................ |
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| Heidelberg, Germany |  |  |
|  |  |  |
| For DKFZ: |  | For RECIPIENT: |
| Deutsches Krebsforschungszentrum Stiftung des öffentlichen Rechts |  | (Name of Institution) |
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|  |  |  |
| ………………………………………. |  | ………………………………………. |
| Name: Dr. Ruth Herzog |  | Name: RECIPIENT SCIENTIST |
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|  |  |  |
|  |  | ………………………………………. |
|  |  | Name:Legal representative of RECIPIENT |