National Cancer Institute

DCTD Division of Cancer Treatment and Diagnosis

Topoisomerase 1 (Top1) Immunoassay Reagent Request Form

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Material Transfer Agreement: Reagents to Support Sponsored Clinical Trials and Approved Preclinical Studies

This Material Transfer Agreement ("**MTA**") has been designed for use by the **National Cancer Institute** ("**NCI**"), an agency of the United States Government (Government), to transfer materials to institutions participating in NCI-sponsored clinical trials and NCI-approved preclinical studies.

Provider: National Cancer Institute

Recipient: _____

Authorized Users: Recipient's employees supporting the activities under this Agreement who have completed the assay training course sponsored by the Provider and received a certificate of completion.

List All Certified Assay Operators (Authorized Users) and their Training Certificate Numbers:

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

WHEREAS the Provider has developed assay reagents for the assessment of the behavior and abundance of the target protein specified in Appendix 2; and

WHEREAS Leidos Biomedical Research, Inc, the Operations and Technical Support contractor to the National Cancer Institute at Frederick, will assist Provider in the supply chain management by providing assay reagents in a standardized and qualified form, and other administrative and technical support of activities described by this MTA; and

WHEREAS, the Recipient is interested in utilizing the reagents to assess the behavior and abundance of the specified target protein in experiments conducted during clinical studies sponsored by the Provider or in preclinical studies approved by the Provider;

The Provider and Recipient agree to the following:

1. Provider agrees to transfer to Recipient the assay reagents designated in Appendix 2 (henceforth "Research Material"):

2. THIS RESEARCH MATERIAL MAY NOT BE USED IN HUMAN SUBJECTS. The Research Material will only be used for research purposes by Authorized Users in the Recipient's laboratories for the research project described below, under suitable containment conditions. This Research Material will not be used by Recipient 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 including, as applicable, rules and regulations pertaining to the study of Human Subjects within the meaning of 45 C.F.R. Part 46, or of materials collected from Human Subjects and pertaining to Humane Care and Use of Laboratory Animals (*LINK*).

3. This Research Material will be used by Recipient solely to determine the designated target protein levels in tissues obtained from humans, approved preclinical study(s), or in proficiency sample sets from appropriate models (henceforth "Research Project").Check box(s) below for the indicated use of assays.

☐ Proficiency samples

☐ Clinical Trial samples (provide trial information)

☐ Preclinical samples (provide study design information)

The number of Packs that a Certified Assay Site may receive is limited to the number of specimens collected based on patient accrual or preclinical study design.

CLINICAL TRIAL INFORMATION

(*if more than one trial duplicate table below and attached as an Appendix)

Clinical Trial Title:
Protocol ID (NCT):
CTEP Protocol ID:
Internal Protocol ID:
Other NCI Protocol ID:
NCI Grant/Contract Number Supporting Trial:

PRECLINICAL STUDY INFORMATION

Provide Institutional Animal Care and Use Approval Documentation/Numbers:

(*if more than one study duplicate table below and attached as an Appendix)

Preclinical Study Title:
Protocol (Animal Care/Use Review) ID:
Drugs /Doses used:
animals:
specimens:
Other relevant Information::

4. To the extent permitted by law, Recipient agrees to treat in confidence, for a period of three (3) years from the date of its disclosure, any of Provider's written information about this Research Material that is stamped "CONFIDENTIAL," except for information that was previously known to Recipient, as demonstrated by competent evidence, or that is or becomes publicly available, or which is disclosed to Recipient without a confidentiality obligation, or for which the Recipient has obtained the Provider's written consent to disclose. Any oral disclosures from Provider to Recipient shall be identified as being CONFIDENTIAL by written notice delivered to Recipient within thirty (30) days after the date of the oral disclosure.

5. This Research Material represents a significant investment on the part of Provider and is considered proprietary to Provider. Recipient therefore agrees to retain control over this Research Material and further agrees not to allow unauthorized users access. Recipient agrees it will ensure that only the Authorized Users operating under the Recipient's control are permitted to use the Research Materials. 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 Recipient will dispose of the Research Material or return the Research Material to Provider at Provider's expense as directed by Provider. The returned Research Material may be subjected to quality analysis by the Provider to assess stability in the field. Such disposal or return shall be performed in compliance with all applicable statutes and regulations.

6. 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.

7. 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. Recipient agrees not to claim, infer, or imply endorsement by the Provider or by Leidos Biomedical Research, Inc, of the Recipient's Research Project to include their institution or personnel conducting the Research Project. Unless prohibited by law from doing so, Recipient agrees to hold the Provider and Leidos Biomedical Research, Inc, harmless and to indemnify the Provider and Leidos Biomedical Research, Inc, for all liabilities, demands, damages, expenses and losses arising out of Recipient's use for any purpose of the Research Material.

8. The Recipient will provide selected assay performance data obtained using the Research Materials (henceforth "Data") to the Provider. The Data provided to the Provider will include raw data and calculated results of the analyses of standard curves and controls. In no case will Recipient deliver Data to the Provider later than the earlier of:

    a. 30 days following depletion of each reagent package; or

    b. the date of completion of each clinical trial or preclinical study described in the Research Plan.

    Recipient will not transmit to the Provider or Provider's contractors any information describing individual patient samples, or information that could be used to identify an individual human patient. Likewise, experimental assay results from the preclinical studies are not to be transmitted.

    Data will be owned by the party that generates the Data.

    The Provider and Leidos Biomedical Research, Inc may use the Data to monitor the consistency of assay performance between sites, for its own internal analyses, and to support regulatory filings. The Provider and Recipient agree that the Provider may publically disclose the Data, or direct Leidos Biomedical Research, Inc, to do so, to support the Provider's goals associated with the Pharmacodynamic Assay Program. The Provider represents that it shall not disclose the name of the Recipient in any public disclosure unless:

    a. authorized in writing by Recipient; or

    b. as required by law, court order, or agency regulation or policy.

9. Recipient may publish or otherwise publically disclose the results of the Research Project in accordance with the following conditions:

    a. Drafts of Recipient's planned presentation of Data must be provided to Provider for courtesy review at least thirty (30) days prior to submission to a publisher or meeting organizer.

    b. Recipient's press releases and other publicity announcements concerning the Research Project must be provided to Provider for review and comment no less than seven (7) days prior to release.

    c. In all presentations or written publications concerning the Research Project, Recipient will acknowledge Provider's contribution of this Research Material, unless requested otherwise, using the following wording:

    "Material(s) were used in the pharmacodynamic assay according to the SOPs from the Division of Cancer Treatment and Diagnosis at the National Cancer Institute, and were supplied to the Provider in qualified form by Leidos Biomedical Research, Inc . *This does not claim, infer, or imply an endorsement or recommendation of the material by the Investigator, the NCI, or* Leidos Biomedical Research, Inc.*"*

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

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

12. In the event that the terms of this Agreement conflict with the terms of any other Agreement between Provider and Recipient concerning the Research Project, then the identification of the prevailing term shall be at the sole discretion of the Provider.

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

SIGNATURES APPEAR ON THE FOLLOWING PAGE

ACCEPTED AND AGREED

FOR THE RECIPIENT

Recipient's Official Mailing Address

Authorized Signature for Recipient

Printed Name and Title

Date

FOR THE PROVIDER

National Cancer Institute

Provider's Official Mailing Address

James Doroshow, M.D.

Director, Division of Cancer Treatment and Diagnosis

National Cancer Institute

National Cancer Institute

Technology Transfer Center

609 Medical Center Drive, Suite 1E530, MSC 9702

Bethesda, MD 20892-9702

Date

and

Thomas P. Clouse, J.D., M.F.S., CLP

Technology Transfer Specialist

Printed Name and Title

Date

CONTACT INFORMATION

Recipient's MTA Request - Contact Information and Address

Karen Dawn Gray, Ph.D., PMP

Senior Project Manager II

Applied/Developmental Directorate

Support to the Project Management Office for DCTD

Leidos Biomedical Research, Inc.

Frederick National Laboratory for Cancer Research

9609 MEDICAL CENTER DR, RM 4-W504, Rockville, MD, 20850

MSC 9731

Phone: 240-276-5998 (Office); 240-409-0694 (Blackberry)

E-mail: grayk2@mail.nih.gov

(Direct interoffice and USPS mail to: 9609 MEDICAL CENTER DR, RM 4-W504, MSC 8300, BETHESDA MD 20892)

Recipient's Standard Curve and Control Data (electronic files are acceptable) - Contact Information and Address

Kate Ferry-Galow, Ph.D.

Principal Scientist

Clinical Pharmacodynamic Biomarkers Program

Applied/Developmental Research Directorate

Frederick National Laboratory for Cancer Research

Leidos Biomedical Research, Inc.

1050 Boyles Street

Frederick, MD 21702

Phone: Office 301-228-4665; Mobile 240-409-8519

E-mail: ferrygalowkv@mail.nih.gov

Unused Reagents - Return Shipping Address

Kate Ferry-Galow, Ph.D.

See address above.

Appendix 1: Expanded Policy

1. Each reagent request will require a new Material Transfer Agreement (Appendix 2) or an amendment to a current MTA.
2. One introductory kit will be provided to all certified attendees of the assay training course.
3. Additional free assay reagents will be provided only to institutions participating in NCI-sponsored clinical trials or carrying out NCI/DCTD approved preclinical studies for which the assay has been designed. Each reagent request will require a new Material Transfer Agreement or amendment. No more than 3 reagent packs will be distributed per request.
4. Free reagents will not be provided to commercial entities for testing in non-NCI clinical trials or preclinical studies not approved by NCI/DCTD. The companies will be referred to commercial sources for their critical reagents. The acceptable performance ranges and expected variability of the assay will be posted on the Biomarker Website and published in peer-reviewed journals which provide information for performance comparisons by public entities. Exceptions such as listed below will be considered on a case-by-case basis and will require NCI/DCTD approval to implement.
    a. Standards, controls, or calibrators may be provided to companies for head-to-head comparison of the performance of their test to that of NCI/DCTD.
    b. If the NCI/DCTD initiates a CRADA for joint pharmaceutical trials that require a NCI/DCTD PD Assay, then free reagents may be provided if supply is sufficient.
5. Certifications and human and animal use assurances and protocol information are to be listed on the Reagent Request form.
6. If reagents are to be used for analysis of specimens from more than one clinical trial or approved preclinical study, complete information for the additional trial(s) or preclinical study design(s) are to be filled out, and if necessary, attached as an Appendix to the request.
7. A completed reagent form and MTA are to be submitted to Karen Gray (grayk2@mail.nih.gov).

MTA Questions contact:

Karen Dawn Gray, Ph.D., PMP

Phone: 240-276-5998 (Office); Mobile 240-409-0694 (Blackberry) E-mail: grayk2@mail.nih.gov

Assay Reagent Questions contact:

Kate Ferry-Galow, Ph.D.

Phone: 301-228-4665 (Office); Mobile 240-409-8519 E-mail: ferrygalowkv@mail.nih.gov

Appendix 2: Top1 Immunoassay Reagent Request Form

Clinical Investigator Information

Requestor Last Name	First Name	M.I.
Title	Institution	
Street Address		Unit # (Suite, Rm)
City	State	Zip Code
Primary Phone #	Alternate Phone #	
E-mail Address		

Policy and Material Transfer Agreement (MTA)

The Material list comprising the qualified reagent pack is outlined in Appendix 3. One introductory kit will be provided to all certified trainees of the assay training course. Additional free reagents for pharmacodynamic analysis of specimens will be provided to institutions participating in National Cancer Institute (NCI) sponsored clinical trials and to institutions that have received the NCI Division of Cancer Treatment and Diagnosis (DCTD) approval for specific preclinical studies for which the assay has been designed. Details of the clinical and/or preclinical study(s) are to be included in the original MTA and amendments. No more than 3 reagent packs will be distributed per request.

Each reagent request will require a new MTA or an amendment to a current MTA. The completed reagent request form and MTA should be submitted to Karen Gray (grayk2@mail.nih.gov) for processing.

Material Transfer Agreement: Date Effective:_____

Top1 Assay Certificate #	**Issue Date:**

Purpose of order (check all appropriate):

- ☐ Free Introductory Kit for Trainee
- ☐ Support of NCI-Sponsored Clinical Trial(s)
- ☐ Support of NCI-Approved Preclinical Study(s)
- ☐ Proficiency Testing

Number of Top1 Immunoassay Reagent Packs Requested: _____ (no more than 3 reagents packs/request)

- Each reagent pack is sufficient for three (3) 96-well ELISA plates – see Appendix 3.
- The number of Packs that a Certified Assay Site may receive is limited to the actual accrual and number of specimens collected for early stage clinical trial(s) or approved preclinical study(s), depending on NCI's supply.
- Proficiency Panels provided upon request.

Brief Justification for Number of Packs Being Requested for Clinical/Preclinical Studies (e.g., anticipated accrual x sampling design of the trial; or number of preclinical specimens):

Shipping Contact and Address

Last Name	First Name	M.I.
Title	Institution	
Street Address		Unit # (Suite, Rm)
City	State	Zip Code
Primary Phone #	Alternate Phone #	
E-mail Address		

Comments:

For Internal Use Only

Date of Request	Number of Reagent Packs Requested
Date of Shipment	Number of Packs Shipped
Batch Number of Pack(s)	Express Mail Tracking Number

Comments:

NCI/DCTD Approval Signature Date

LEIDOS (PADIS/IQC) Laboratory Shipper Signature Date

APPENDIX 3: Top1 Immumoassay List of Materials

Description: Each pack contains vials of qualified critical reagents, standards, and controls to ensure valid measurement of Top1 levels in tissue or isolated cells when following the NCI/DCTD-approved SOPs for the Top1 Immunoassay (see DCTD Biomarkers at http://dctd.cancer.gov). Sufficient material is provided in single-use or multi-use vials (noted below) to perform three (3) 96-well Top1 Immunoassays. The reagents in the pack are matched to each other's performance, and therefore must only be used together to perform a valid assay. The individual reagents from different batches of packs cannot be used together.

Recombinant Top1 standard, tumor lysate control, HRP goat anti-rabbit polyclonal antibody, 96-well plates, and plate sealers are stable for up to 1 year when stored as specified. Anti- Top1 monoclonal and polyclonal antibodies and chemiluminescent substrate are stable for only 3 months. Other replacement reagents can be requested as needed.

There is a limit of 3 Critical Reagent Packs per Certified Assay Site in addition to that provided during the NCI training course. Each reagent request will require a new MTA or an amendment to a current MTA.

Item	*Reagent Name*	*Description*	*Storage Conditions*	*Number*
1	Collection Tubes	Precellys Ceramic Bead Collection Tubes, 2.8 mm beads, 2.0-mL reinforced tubes	Room temperature	18
2	Phosphate Buffered Saline/Casein Block and Diluent	5X PBS-Casein is a concentrated qualified lot of diluent buffer	2°C to 8°C	1 Multi-use
3	PDA II Antibody Coating Buffer	Qualified lot of coating buffer for 96-well plate	2°C to 8°C	1 Multi-use
4	rTop1 Standard	Purified recombinant Top1 of known concentration to set up standard curve.	-80°C	3 Single-use
5	Tumor Lysate Control	Cultured MCF-7 tumor cell extract with known concentration of Top1.	-80°C	3 Single-use
6	Top1 Mouse mAb	Capture anti-Top1 mouse monoclonal antibody that binds Top1 molecules in crude extracts.	2°C to 8°C	1 Multi-use
7	Top1 Rabbit pAb	Anti-Top1 rabbit polyclonal antibody to sandwich the Top1-containing antigens.	-20°C	1 Multi-use
8	Goat Anti-Rabbit HRP-Conjugate	HRP (horseradish peroxidase) enzyme-linked detection antibody that binds to the Top1 rabbit pAb.	2°C to 8°C	1 Multi-use
9	Tween 20	Qualified Tween 20 aqueous solution, 10% w/v	2°C to 8°C	3 Single-use
10	Chemiluminescent Substrate Pico Stable Peroxide and Luminol/Enhancer Solutions	Luminescent substrate solution for quantifying Top1antibody signal. The HRP enzyme uses this substrate and hydrogen peroxide to produce a product that emits light that can be measured using enhanced chemiluminescence.	Room temperature	1 set Multi-use