National Cancer Institute

DCTD Division of Cancer Treatment and Diagnosis

# γH2AX Immunofluorescence Assay for Biopsy Slides
# 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 components of the qualified reagent pack are outlined in Appendix 1. Free reagents for pharmacodynamic analysis of patient specimens will be provided only to institutions participating in NCI-sponsored clinical trials for which the assay has been designed, with the exception that one introductory kit will be provided to all certified trainees of the assay training course. Each reagent request will require a new MTA (Appendix 2) or an amendment to a current MTA. If the reagents are to be used for analysis of specimens from more than one clinical trial, attach clinical trial information for the additional trial(s) to this request. See Appendix 3 for additional policy information. he completed reagent request form and MTA should be submitted to Karen Gray (grayk2@mail.nih.gov).

Material Transfer Agreement: **Date Effective**:_____

## *Clinical Trial Information*

Purpose (check one): ❒ Free Introductory Kit for Trainee ❒ Support of NCI-Sponsored Clinical Trial(s) ❒ New Platform Studies ❒ Other (Special Projects):

Clinical Trial Title:

Protocol ID (NCT): | CTEP Protocol ID:

Internal Protocol ID: | Other NCI Protocol ID:

NCI Grant/Contract Number Supporting Trial:

Certified Assay Operator: | Director/Supervisor:

γH2AX IFA Certificate #: | Issue Date:

Number of γH2AX Immunofluorescence Assay Reagent Packs Requested: _____

- Each reagent pack is sufficient for the analysis of slides from 3 patients - see page 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), depending on NCI's supply
- Equivalence Packs provided upon request.

Justification for Number of Packs Being Requested (e.g., anticipated accrual x sampling design of the trial):

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

## *Shipping Contact and Address*

| Last Name | First Name | M.I. |
|---|---|---|
| Institution | | |
| Street Address | | Unit # (Suite, Rm) |

| City | State | Zip Code | Country |
|---|---|---|---|
| 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:

DCTD Approval Signature

NCTVL Shipper Signature

# Appendix 1: Critical Reagent Pack for the γH2AX Immunofluorescence Assay for Biopsy Slides

**Description:** Each pack contains vials/units of qualified critical reagents and controls to ensure valid measurement of γH2AX levels in paraffin-embedded tumor biopsies when following the DCTD-approved SOPs for the γH2AX Immunofluorescence Assay (see DCTD Biomarkers at http://dctd.cancer.gov). Sufficient material is provided in single-use or multi-use units (noted below) to perform the γH2AX Immunofluorescence Assay with 3 sets of patient samples (2 biopsies per patient). The reagents include a 2-fold surplus, so under optimal conditions 6 sets of patient samples can be assayed. 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.

The fresh-frozen murine testes are stable for up to 1 month when stored as specified. The γH2AX biotin conjugate antibody and Alexa Fluor 488-streptavidin conjugate antibody are stable for up to 3 months when stored as specified. The calibrator/control slides are stable indefinitely when stored as specified.

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), depending on NCI's supply. Each reagent request will require a new Material Transfer Agreement (Appendix 2) or an amendment to a current MTA

| *Item* | *Reagent Name* | *Description* | *Storage Conditions* | *No. of Vials/Units* | *Unit size* |
|---|---|---|---|---|---|
| 1 | Fresh-Frozen Murine Testes | Positive control tissue for clinical slide preparation. | -80°C | 6<br>Single-use | 1/4 testis |
| 2 | Anti-γH2AX Biotin Conjugate | Biotin-conjugated primary antibody that specifically recognizes the γH2AX antigen in FFPE tissue. | -20°C | 1<br>Multi-use | 228 µL |
| 3 | Streptavidin, Alexa Fluor 488 Conjugate | Alexa Fluor 488 linked detection antibody that binds the γH2AX-biotin conjugate antibody. | -20°C | 1<br>Multi-use | 150 µL |
| 4 | Calibrator/Control Slides | One slide contains 3 calibrator sections of cell line pellets with known %NAP γH2AX ranges and a positive and negative control section. | 2°C to 8°C in desiccator; away from volatiles | 12<br>Single-use | 1 slide |
| 5 | DAPI | DAPI nuclear stain for fluorescent counterstaining of DNA during fluorescence microscopy. | -20°C | 1<br>Multi-use | 10 µL |

An Equivalence Pack with known γH2AX levels for laboratory equivalence and system verification is available upon request. The Equivalence Pack will include 4 calibrator/control slides to validate system equivalence and a set of xenograft samples with known γH2AX levels to tune the laboratory's system and confirm that the validated system can read tissue samples in a range that is relevant to the supplied calibrator/control slides. The Equivalence Pack will also include lot-matched vials of γH2AX biotin conjugate antibody, Alexa Fluor 488-streptavidin conjugate antibody, and DAPI.

# Appendix 2: Material Transfer Agreement: Reagents to Support Sponsored Clinical Trials

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.

**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 reagents for the assessment of the behavior and abundance of the histone H2AX protein phosphorylated at Ser139 designated as γH2AX; and

WHEREAS SAIC-Frederick, the Operations and Technical Support contractor to the Frederick National Laboratory for Cancer Research, 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 histone H2AX protein phosphorylated at Ser139 designated as γH2AX in experiments conducted during clinical studies sponsored by the Provider;

**The Provider and Recipient agree to the following:**

1. Provider agrees to transfer to Recipient the γH2AX assay reagents check marked below (henceforth "Research Material"):

   A. As specified in the Critical Reagent Pack

   ☐ Critical Reagent Pack components

   B. Individual components (check all that apply):

   ☐ Standards: Synthetic or purified preparation to use as the analytical calibrator
   ☐ Controls: Positive and negative control preparations
   ☐ Capture analyte specific antibody
   ☐ 2nd analyte specific antibody
   ☐ Conjugated species specific anti-immunoglobulin antibody
   ☐ Light emitting substrate
   ☐ Data analysis software
   ☐ Other reagents or supplies

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.

3. This Research Material will be used by Recipient solely to determine γH2AX levels in tissues obtained from humans or in proficiency sample sets from appropriate models (henceforth "Research Project") in support of the following NCI-sponsored clinical trial(s). Check box below for the indicated use of assays.

☐ Proficiency samples

☐ Clinical Trial samples (provide trial information)

The number of Packs that a Certified Assay Site may receive is limited to the actual patient accrual and number of specimens collected for early stage clinical trial(s) and on approval and availability of reagents at NCI.

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

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

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

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 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 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 or return the Research Material as directed by Provider. 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 Government of the United States of America (hereinafter referred to as "Government") or by SAIC-Frederick of the Research Project, the institution or personnel conducting the Research Project or any resulting product(s). Unless prohibited by law from doing so, Recipient agrees to hold the Government and SAIC-Frederick harmless and to indemnify the Government and SAIC-Frederick 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 its data obtained using the Research Materials (henceforth "Data") to the Provider upon request. 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 described in the Research Plan.

    The Data provided to the Provider will include raw data and calculated results of the analyses of standard curves, calibrators, and controls. 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.

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

    The Provider and SAIC-Frederick 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 SAIC-Frederick 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 SAIC-Frederick. This does not claim, infer, or imply an endorsement or recommendation of the material by the Investigator, the NCI, or SAIC-Frederick."*

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
6120 Executive Blvd., EPS 450
Rockville, MD 20852

Date

and

Authorized Signature for Provider

Printed Name and Title

Date

# CONTACT INFORMATION

### *Recipient's MTA Request - Contact Information and Address*

Karen Dawn Gray, Ph.D., PMP (Contractor)
SAIC-Frederick, Inc.
Frederick National Laboratory for Cancer Research
6116 Executive Plaza Blvd., Suite 109, Mail Drop 8300
Rockville, MD, 20892-8300
Phone: Office 301-594-1188; Blackberry 301-978-6994
Fax: 301-443-7001
Email: grayk2@mail.nih.gov

### *Recipient's Data (electronic files are acceptable) - Contact Information and Address*

Jiuping Ji, Ph.D.
SAIC-Frederick, Inc.
National Institutes of Health
37 Convent Dr., Bldg 37/Rm 1048
Bethesda, MD 20814
Phone: 301-443-2094
Email: jijiupi@mail.nih.gov

### *Unused Reagents - Return Shipping Address*

Jiuping Ji, Ph.D.
See address above.

# Appendix 3: 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. 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), depending on NCI's supply.
4. Free reagents will not be provided to commercial entities for testing in non-NCI clinical trials. 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. There may be possible exceptions such as listed below, but further discussion is needed before implementation.
    a. If company personnel attend assay training sponsored by NCI/SAIC-F, each trainee will quality for one free reagent packet.
    b. On a case-by-case basis, standards, controls, or calibrators may be provided to companies for head-to-head comparison of the performance of their test to that of NCI/SAIC-F.
    c. If the FDA initiates a CRADA for joint pharmaceutical trials that require a DCTD PD Assay, then free reagents may be provided if supply is sufficient
5. Certifications and human and animal 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, complete information for the additional trial or trials 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).

### *Questions contact:*

Karen Dawn Gray, Ph.D., PMP (Contractor)

Phone: Office 301-594-1188; Blackberry 301-978-6994

E-mail: grayk2@mail.nih.gov