

DATA USE CERTIFICATION AGREEMENT

CALB40601: Randomized Phase 3 Trial of Paclitaxel Combined with Trastuzumab, Lapatinib, or Both as Neoadjuvant Treatment of HER2-Breast-Positive Breast Cancer

For use with the National Cancer Institute's Cancer Therapy Evaluation Program (CTEP)

NCT#: NCT00770809

NCI Collaborator(s): Novartis

INTRODUCTION AND STATEMENT OF POLICY

The National Institutes of Health (NIH) has established NIH-designated data repositories (e.g., database of Genotypes and Phenotypes (dbGaP), Sequence Read Archive (SRA), NIH Established Trusted Partnerships) for securely storing and sharing controlled-access human data submitted to NIH under the [NIH Genomic Data Sharing \(GDS\) Policy](#). Because the volume of human genomic and phenotypic data contained in these repositories is substantial and, in some instances, potentially sensitive (e.g., data related to the presence or risk of developing particular diseases or conditions and information regarding family relationships or ancestry), data must be shared in a manner consistent with the research participants' informed consent, and the confidentiality of the data and the privacy of participants must be protected.

Access to human genomic data will be provided to approved research investigators who, along with their institutions have certified their agreement with the expectations and terms of access detailed below. It is the intent of NIH that Approved Users of controlled-access datasets obtained through the Data Access Request (DAR) recognize any restrictions on data use established by the submitting institutions ("Submitting Institutions") through the Institutional Certification and stated on the dbGaP study page.

Definitions of terminology used in this document are found in the Appendix.

The parties to this Agreement include: the principal investigator (PI) who requested and was approved by NCI access to the genomic study dataset (an "Approved User"), the PI's home institution as represented by the Institutional Signing Official designated through the electronic research administration (eRA) Commons system (the "Requester"), and the relevant NIH Institute or Center (IC), which for this Agreement is the National Cancer Institute (NCI). The effective date of this Agreement shall be the project approval date, as specified on the Extramural NCI Data Access Committee (eNCI DAC) approval notification (see: <https://epi.grants.cancer.gov/dac/charter.html>).

TERMS OF ACCESS

1. Research Use

The Requester agrees that if access is approved, (1) the Approved User named in the DAR and (2) those named in the "Senior/Key Person Profile" section of the DAR, including the Information

Technology Director and any trainee, employee, or contractor¹ working on the proposed research project under the direct oversight of these individuals, shall become an Approved User of the requested dataset(s). Research use will occur solely in connection with the approved research project described in the DAR, which includes a 1-2 paragraph description of the research objectives and design. Investigators interested in using cloud computing² for data storage and analysis must indicate in their Data Access Request (DAR) that they are requesting permission to use cloud computing and identify the cloud service provider (CSP)³ or providers and/or Private Cloud System (PCS) that they propose to use. They must also submit a Cloud Computing use statement as part of the DAR that describes the type of service and how it will be used to carry out the proposed research described in the research use statement of the DAR. If the Approved User plans to collaborate with investigators outside the Requester, the investigators at each external site must submit an independent DAR using the same project title and research use statement, and if using the cloud, Cloud Computing use statement. New uses of these data outside those described in the DAR will require submission of a new DAR; modifications to the research project will require submission of an amendment to this application (e.g., adding or deleting Requester Collaborators from the Requester, adding datasets to an approved project). Access to the requested dataset(s) is granted for a period of **one (1) year** as defined below.

Contributing Investigators, or their direct collaborators, who provided the data or samples used to generate controlled-access datasets subject to the GDS Policy and who have Institutional Review Board (IRB) approval, if applicable, for broad use of the data, are exempt from the limitation on the scope of the research use as defined in the DAR.

NCI Specific Terms:

See Article 7, below for CTEP IP Option and publication review terms.

Data Use Limitations:

The eNCI DAC recognizes the [Data Use Limitations](#) of each consent group stated on the dbGaP study page (*to show the content, mouse over title of the consent group in the Authorized Access*

¹ If contractor services are to be utilized, the principal investigator (PI) requesting the data must provide a brief description of the services that the contractor will perform for the PI (e.g., data cleaning services) in the research use statement of the DAR. Additionally, the Key Personnel section of the DAR must include the name of the contractor's employee(s) who will conduct the work. These requirements apply whether the contractor carries out the work at the Approved User's facility or at the contractor's facility. In addition, the Approved User is expected to include in any contract agreement requirements to ensure that any of the contractor's employees who have access to the data adhere to the [GDS Policy](#), this Data Use Certification Agreement, and the [NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy](#). Note that any scientific Collaborators, including contractors, who are not at the Requester must submit their own DAR.

² The National Institute for Standards and Technology (NIST) defines cloud computing as a model for enabling ubiquitous, convenient, on-demand network access to a shared pool of configurable computing resources (e.g., networks, servers, storage, applications, and services) that can be rapidly provisioned and released with minimal management effort or service provider interaction. For more information, see: <http://csrc.nist.gov/publications/nistpubs/800-145/SP800-145.pdf>.

³ NIST defines a cloud service provider as a company that offers some component of cloud computing to other businesses or individual, typically Infrastructure as a Service (IaaS), Software as a Service (SaaS) or Platform as a Service (PaaS). For more information, see: <http://csrc.nist.gov/publications/nistpubs/800-145/SP800-145.pdf>

section).

2. Requester and Approved User Responsibilities

The Requester agrees that the Approved User has reviewed and understands the principles for responsible research use and data management of the genomic datasets as defined in the [NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy](#). The Requester and Approved User further acknowledge that they are responsible for ensuring that all uses of the data are consistent with national, tribal, and state laws and regulations, as appropriate, as well as relevant Requester policies and procedures for managing sensitive genomic and phenotypic data. The Requester certifies that the Approved User is in good standing (i.e., no known sanctions) with the Requester, relevant funding agencies, and regulatory agencies and is eligible to conduct independent research (i.e., is not a postdoctoral fellow, student, or trainee). The Requester and any Approved User may use the dataset(s) only in accordance with the parameters described on the dbGaP website for the appropriate research use, as well as any limitations on such use, of the dataset(s) and as described in the DAR and as required by law.

The Approved User agrees to submit either a Project Renewal or Project Close-out request prior to the expiration date of the one-year data access period. The Approved User also agrees to submit an annual progress update or a final progress report prior to the one-year anniversary of the DAR, as described under Article 9 (*Research Use Reporting*) below. Failure to submit a Project Renewal or to complete the Project Close-out process, including confirmation of data destruction by the Requester through its Institutional Signing Official, may result in termination of all current data access and/or suspension of the Approved User and all associated personnel and Requester Collaborators from submitting new DARs for a period to be determined by NIH. Repeated violations or unresponsiveness to NIH requests may result in further compliance measures affecting the Requester.

An Approved User who has access to personal identifying information for research participants in the original study at the Requester or through their Requester Collaborators may be required to have IRB approval. By approving and submitting the attached DAR, the Requester through its Institutional Signing Official provides assurance that relevant institutional policies and national, tribal, and state laws and regulations, as applicable, have been followed, including IRB approval if required. The Institutional Signing Official also assures through the approval of the DAR that other institutional departments with relevant authorities (e.g., those overseeing human subjects research, information technology, or technology transfer) have reviewed the relevant sections of the NIH GDS Policy and the associated procedures and will uphold the principles defined.

Requester acknowledges that NIH anticipates that controlled-access datasets subject to the GDS Policy will be updated with additional information. Unless otherwise indicated, all statements herein are presumed to be true and applicable to the access and use of all versions of these datasets.

3. Public Posting of Approved User's Research Use Statement

Approved User agrees that information about themselves and their approved research use will be posted publicly on the dbGaP website. The information includes the Approved User's name and Requester, project name, research use statement, and a non-technical summary of the research use statement. In addition, and if applicable, this information may include the Cloud Computing use statement and name of the CSP or PCS. Citations of publications resulting from the use of controlled-access datasets obtained through this DAR may also be posted on the dbGaP website.

4. Non-Identification

Approved User agrees not to use the requested datasets, either alone or in concert with any other information, to identify or contact individual participants from whom data and/or samples were collected. This provision does not apply to research investigators operating with specific IRB approval, pursuant to 45 CFR 46, to contact individuals within datasets or to obtain and use identifying information under an IRB approved research protocol. All investigators including any Approved User conducting "human subjects research" within the scope of 45 CFR 46 must comply with the requirements contained therein.

5. Non-Transferability

The Requester and Approved User agree to retain control of NIH controlled-access datasets obtained through the attached DAR and any derivatives⁴ of controlled-access datasets and further agree not to distribute controlled-access datasets and derivatives of controlled-access datasets to any entity or individual not identified in the submitted DAR. If the Approved User is provided access to controlled-access datasets subject to the GDS Policy for inter-institutional collaborative research described in the research use statement of the DAR, and all members of the collaboration are also Approved Users through their home institution(s), data obtained through the attached DAR may be securely transmitted within the collaborative group. Each Approved User will follow all data security practices and other terms of use defined in this Agreement, the [NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy](#) and the Requester's IT security requirements and policies.

The Requester and Approved User acknowledge responsibility for ensuring the review and agreement to the terms within this Agreement and the appropriate research use of controlled-access data obtained through the attached DAR and any derivatives of controlled-access datasets by research staff associated with any approved project, subject to applicable laws and regulations. Requester and Approved User agree that controlled-access datasets obtained through the attached DAR and any derivatives of controlled-access datasets, in whole or in part, will not be sold to any individual or organization at any point in time for any purpose.

Approved User agrees that if they change institutions during the access period they will complete the DAR close-out process before moving to their new institution. A new DAR and Data Use Certification Agreement, in which the new institution agrees to the [GDS Policy](#), must be approved by the eNCI DAC before controlled-access data may be re-accessed. As part of the close-out process, all copies and

⁴ Any data containing individual-level information that are generated or inferred from controlled-access datasets (e.g. imputed or annotated data) obtained from NIH-designated data repositories (e.g., dbGaP).

versions of the datasets retrieved from NIH-designated controlled-access databases as well as any derivatives of controlled-access datasets stored at the Requester and/or CSP must be destroyed and destruction confirmed by the Institutional Signing Official, as described below.

6. Data Security and Data Release Reporting

The Requester and any Approved User, including the Requester's IT Director, have reviewed and agree to manage the requested controlled-access dataset(s) and any derivatives of controlled-access datasets according to NIH's expectations set forth in the current [NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy](#) and the Requester's IT security requirements and policies, and that the Institution's IT security requirements and policies are sufficient to protect the confidentiality and integrity of the NIH controlled-access data entrusted to the Requester.

If approved by NIH to use cloud computing for the proposed research project, as outlined in the Research and Cloud Computing Use Statements of the DAR, the Requester will ensure that the IT Director has reviewed and understands the cloud computing guidelines in the [NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy](#).

Requester and the Approved User agree to notify the eNCI DAC of any unauthorized data sharing, breaches of data security, or inadvertent data releases that may compromise data confidentiality within 24 hours of the incident being identified. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in place to define and remediate the situation fully. Within 3 business days of the eNCI DAC notification, the Requester agrees to submit to the eNCI DAC a detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.

All notifications and written reports of data security incidents should be sent to:

eNCI DAC URGENT email: ncidac-urgent@mail.nih.gov

GDS mailbox: gds@mail.nih.gov

NCI or another entity designated by NIH may, as permitted by law, also investigate any data security incident. Approved User agrees and will require their associates to agree to support such investigations and provide information, within the limits of applicable local, state, and federal laws and regulations. In addition, Requester and Approved User agree to work with the eNCI DAC and other components of NIH to assure that plans and procedures that are developed to address identified problems are mutually acceptable and consistent with applicable law.

7. Intellectual Property

I. General Principles: Subject to the terms described in section 7.II., by requesting access to genomic dataset(s), the Requester and Approved User acknowledge the intent of NCI that anyone authorized for research access through the attached DAR will follow the intellectual property (IP) principles in

the [NIH GDS Policy](#) as summarized below:

Achieving maximum public benefit is the ultimate goal of data distribution through the NIH-designated data repositories. The NIH encourages broad use of NIH-supported genotype-phenotype data that is consistent with a responsible approach to management of intellectual property derived from downstream discoveries, as outlined in the NIH [Best Practices for the Licensing of Genomic Inventions](#) and its [Research Tools Policy](#).

The NIH considers these data as pre-competitive and urges Approved User to avoid making IP claims derived directly from the genomic dataset(s). It is expected that these NIH-provided data, and conclusions derived therefrom, will remain freely available, without requirement for licensing. However, the NIH also recognizes the importance of the subsequent development of IP on downstream discoveries, especially in therapeutics, which will be necessary to support full investment in products to benefit the public.

II. Specific IP Requirements for Data Generated Under NCI CTEP Collaborative Agreements:

Certain data requested under this Agreement (“Data”) were generated under a CTEP Collaborative Agreement with a pharmaceutical collaborator (“CTEP Collaborator”) in order to use their drug (“Agent”) in a clinical trial and the Data is, therefore, subject to the terms of the CTEP intellectual property option to CTEP Collaborator (“IP Option”). The Requester and Approved User (collectively referred to as “Institution” in the IP Option) understand and agree that the Data being requested was collected under a CTEP Collaborative Agreement and should an invention, discovery, or innovation arise from the Requester, Approved User, or their authorized associate’s analysis of the Data, the Approved User and the Requester agree to the following:

- A. The IP Option described in this Section A applies to inventions that are described in patent disclosures that claim the use of Data and/or the composition of the Agent and that are conceived or first actually reduced to practice pursuant to clinical or non-clinical studies utilizing the Agent(s) or Data ("Section A Inventions"):

Institution agrees to grant to CTEP Collaborator(s): (i) a royalty-free, worldwide, non-exclusive license for commercial purposes with the right to sub license to affiliates or collaborators working on behalf of CTEP Collaborator for CTEP Collaborator’s development purposes; and (ii) a time limited first option to negotiate an exclusive, or co-exclusive, if applicable, world-wide, royalty bearing license for commercial purposes, including the right to grant sub licenses, subject to any rights of the Government of the United States of America, on terms to be negotiated in good faith by the CTEP Collaborator(s) and Institution. If a CTEP Collaborator accepts the non-exclusive commercial license, the CTEP Collaborator will pay all out of pocket patent prosecution and maintenance costs which will be pro-rated and divided equally among all licensees. If a CTEP Collaborator obtains an exclusive commercial license, in addition to any other agreed upon licensing arrangements such as royalties and due diligence requirements, the CTEP Collaborator will pay all out of pocket patent prosecution

and maintenance costs. A CTEP Collaborator will notify Institution, in writing, if it is interested in obtaining a commercial license to any Section A Invention within three (3) months of the CTEP Collaborator's receipt of a patent application or within six (6) months of receipt of an invention report notification of such a section A invention. In the event that CTEP Collaborator fails to so notify Institution or elects not to obtain an exclusive license, then CTEP Collaborator's option expires with respect to that Section A Invention, and Institution will be free to dispose of its interests in accordance with its policies. If Institution and CTEP Collaborator fail to reach agreement within ninety (90) days, (or such additional period as CTEP Collaborator and Institution may agree) on the terms for an exclusive license for a particular Section A Invention, then for a period of three (3) months thereafter Institution agrees not to offer to license the Section A Invention to any third party on materially better terms than those last offered to CTEP Collaborator without first offering such terms to CTEP Collaborator, in which case CTEP Collaborator will have a period of thirty (30) days in which to accept or reject the offer. If CTEP Collaborator elects to negotiate an exclusive commercial license to a Section A Invention, then Institution agrees to file and prosecute any patent application diligently and in a timely manner and to give CTEP Collaborator an opportunity to comment on the preparation and filing of any such patent application. Notwithstanding the above, Institution is under no obligation to file or maintain patent prosecution for any Section A Invention.

For all Section A Inventions, regardless of CTEP Collaborator's decision to seek a commercial license, Institution agrees to grant CTEP Collaborator a paid-up, nonexclusive, royalty-free, world-wide license for research purposes only. Institution retains the right to make and use any Section A Invention for all non-profit research, including for educational purposes and to permit other educational and non-profit institutions to do so.

- B. The IP Option described in this Section B applies to inventions not covered by Section A, but are nevertheless conceived or first actually reduced to practice pursuant to use of the Data. It also applies to inventions that are conceived or first actually reduced to practice pursuant to NCI CTEP-approved studies that use non-publicly available clinical data or specimens from patients treated with the CTEP-provided Agent (including specimens obtained from NCI CTEP-funded tissue banks) ("Section B Inventions"):

Institution agrees to grant to CTEP Collaborator(s): (i) a paid-up nonexclusive, nontransferable, royalty-free, world-wide license to all Section B Inventions for research purposes only; and (ii) a nonexclusive, royalty-free, world-wide license to (a) disclose Section B Inventions to a regulatory authority when seeking marketing authorization of the Agent, and (b) disclose Section B Inventions on a product insert or other promotional material regarding the Data after having obtained marketing authorization from a regulatory authority. Notwithstanding the above, Institution is under no obligation to file or maintain patent prosecution for any Section B Invention.

- C. The IP Option described in this Section C would apply to inventions made by an Approved User or any other employees or agents of Institution, which are or may be patentable or otherwise protectable, as a result of research utilizing the Data, Agent, or unreleased or non-publicly available clinical data (“Unauthorized Inventions”).

Institution agrees, at CTEP Collaborator's request and expense, to grant to CTEP Collaborator a royalty-free exclusive or co-exclusive license to Unauthorized Inventions. Institution will retain a non-exclusive, non-sub-licensable royalty free license to practice the invention for research use purposes.

- D. Institution agrees to promptly and confidentially notify NCI CTEP (NCICTEPpubs@mail.nih.gov) and CTEP Collaborator(s) in writing of any Section A Inventions, Section B Inventions, and Unauthorized Inventions upon the earlier of: (i) any submission of any invention disclosure to Institution of a Section A, Section B, or Unauthorized Invention, or (ii) the filing of any patent applications of a Section A, Section B, or Unauthorized Invention. Institution agrees to provide a copy of either the invention disclosure or the patent application to the CTEP Collaborator and to NCI CTEP which will treat it in accordance with 37 CFR Part 401. These requirements do not replace any applicable reporting requirements under the Bayh-Dole Act, 35 USC 200-212, and implementing regulations at 37 CFR Part 401.

Any CTEP Collaborator whose Data are provided under this agreement is hereby designated as an intended third party beneficiary of Section 6, Data Access and Data Release Reporting and Section 7, Intellectual Property, in this Agreement signed by the Approved User and/or Requester for access to this Data maintained in dbGaP, and is entitled to independently enforce all rights and obligations under Section 6: Data Access and Data Release Reporting, Section 7: Intellectual Property, and Section 8: Acknowledgement, in this Agreement.

CTEP Collaborator will be provided a statement of the proposed research use for Data in dbGaP, and be provided an opportunity to provide comments within two (2) weeks of CTEP Collaborator receiving a statement of the proposed research use.

8. Research Dissemination and Acknowledgement of Controlled-Access Datasets Subject to the GDS Policy

Subject to section 7.II, as applicable, it is NIH's intent to promote the dissemination of research findings from controlled-access dataset(s) subject to the GDS Policy as widely as possible through scientific publication or other appropriate public dissemination mechanisms. Approved User is strongly encouraged to publish their results in peer-reviewed journals and to present research findings at scientific meetings.

Manuscripts or any form of public disclosure resulting from the Approved User's use of Data will be provided to the appropriate CTEP Collaborator(s) for review at least thirty (30) days

before submission for publication, or seven (7) days before presentation for abstracts and other public disclosures. The Approved User will send manuscripts to NCICTEPpubs@mail.nih.gov, so that NCI may send them to the CTEP Collaborator for comment as described above prior to manuscript submission.

Approved User agrees to acknowledge the Contributing Investigator(s) who submitted data from the original study to dbGaP, the primary funding organization that supported the Contributing Investigators, and the NIH-designated data repository, and the NCI CTEP data repository, in all oral and written presentations, publications and other disclosures resulting from any analyses of controlled-access data obtained through this Agreement. Approved User will include in the acknowledgement the dbGaP accession number(s) to the specific version of the dataset(s) analyzed. The Approved User further agrees to consult with each relevant CTEP Collaborator to determine if the CTEP Collaborator would like to be acknowledged for their contribution of Data to dbGap in the disclosure and, if so, Approved User will provide acknowledgement in the format requested by the CTEP Collaborator. A sample acknowledgment statement for [STUDY NAME] dataset(s) follows:

Funding: The Alliance for Clinical Trials in Oncology NIH-NCI grants U10CA180821 and CALGB U10CA031946; Alliance Statistical Center Grant U10CA180882 and CALGB U10CA33601; Alliance NCTN Biorepository and Biospecimen Resource 5U24CA196171. CALGB 40601 study PI Lisa M. Carey. Carey LA, Berry DA, Cirincione CT, Barry WT, Pitcher BN, Harris LN, Ollila DW, Krop IE, Henry NL, Weckstein DJ, Anders CK, Singh B, Hoadley KA, Iglesia M, Cheang MC, Perou CM, Winer EP, Hudis CA. Molecular Heterogeneity and Response to Neoadjuvant Human Epidermal Growth Factor Receptor 2 Targeting in CALGB 40601, a Randomized Phase III Trial of Paclitaxel Plus Trastuzumab With or Without Lapatinib. J Clin Oncol. 2016 Feb 20;34(6):542-9. doi: 10.1200/JCO.2015.62.1268. Epub 2015 Nov 2. U10CA031946; U10CA180821

Research Use Reporting

To assure adherence to NIH policies and procedures for genomic data, Approved User agrees to provide annual progress updates as part of the annual Project Renewal or Project Close-out processes, prior to the expiration of the one-year data access period. An Approved User who is seeking renewal or close-out of a project agrees to complete the appropriate online forms and provide specific information such as how the data was used, including publications or presentations that resulted from the use of the requested dataset(s), a summary of any plans for future research use (if the Approved User is seeking renewal), any violations of the terms of access described within this Agreement and the implemented remediation, and information on any downstream intellectual property generated from the data. The Approved User also may include general comments regarding topics such as the effectiveness of the data access process (e.g., ease of access and use), appropriateness of data format, challenges in following the policies, and suggestions for improving data access or the program in general. Information provided in the progress updates helps NIH evaluate program activities and may be considered by the NIH GDS governance committees as part of NIH's effort to provide ongoing oversight and management of data sharing activities subject to the GDS Policy.

Note that any inadvertent or inappropriate data release incidents should be reported to the eNCI DAC according to the agreements and instructions under Section 6.

9. Non-Endorsement, Indemnification

The Requester and Approved User acknowledge that although all reasonable efforts have been taken to ensure the accuracy and reliability of controlled-access data obtained through the attached DAR, the NIH, the NCI, the eNCI DAC, and Contributing Investigators do not and cannot warrant the results that may be obtained by using any data included therein. NIH, the NCI, the eNCI DAC, and all contributors to these datasets disclaim all warranties as to performance or fitness of the data for any particular purpose.

No indemnification for any loss, claim, damage, or liability is intended or provided by any party under this agreement. Each party shall be liable for any loss, claim, damage, or liability that said party incurs as a result of its activities under this agreement, except that NIH, as an agency of the United States, may be liable only to the extent provided under the Federal Tort Claims Act, 28 USC 2671 et seq.

10. Termination and Violations

Upon Project Close-out, or expiration/termination of this Agreement, the Approved User agrees to destroy all copies, versions, and derivations of the dataset(s) retrieved from NIH-designated controlled-access databases, on both local servers and hardware, and if cloud computing was used, delete the data and cloud images from cloud computing provider storage, virtual and physical machines, databases, and random access archives, except as required by publication practices, institutional policies, or law to retain them.

The Requester and Approved User understand that the NIH may terminate this Agreement and the eNCI DAC may terminate the DAR including this Agreement and immediately revoke access to all controlled-access datasets subject to the GDS Policy at any time if the Institution or Approved User does not comply with the policies, principles and procedures of the NIH and the eNCI DAC or is in breach of this Agreement.

APPENDIX

DEFINITIONS

Approved User: A user approved by the eNCI Data Access Committee to access one or more NCI datasets for a specified period of time and only for the purposes outlined in the investigator's approved research use statement. The Information Technology (IT) Director indicated on the Data Access Request (DAR), as well as any staff members and trainees under the direct supervision of the PI must each also be an Approved User and abide by the terms laid out in this Data Use Certification Agreement (Agreement).

Approved User Code of Conduct: Key principles and practices agreed to by all research investigators requesting access to controlled-access data subject to the GDS Policy. The elements within the Code of Conduct reflect the terms of access in the Data Use Certification agreement. Failure to abide by the Code of Conduct may result in revocation of an investigator's access to any and all approved datasets. (See https://osp.od.nih.gov/wp-content/uploads/Genomic_Data_User_Code_of_Conduct.pdf)

Cloud Computing: A model for enabling ubiquitous, convenient, on-demand network access to a shared pool of configurable computing resources (e.g., networks, servers, storage, applications, and services) that can be rapidly provisioned and released with minimal management effort or service provider interaction.

Cloud Service Provider (CSP): A company that offers some component of cloud computing to other businesses or individual, typically Infrastructure as a Service (IaaS), Software as a Service (SaaS) or Platform as a Service (PaaS).

Contributing Investigator: An investigator who submitted a genomic dataset to an NIH designated data repository (e.g., dbGaP).

CTEP Collaborative Agreement is the binding document between the National Cancer Institute's Cancer Therapy Evaluation Program (CTEP) and a pharmaceutical collaborator (CTEP Collaborator) or between a clinical trial site and pharmaceutical CTEP Collaborator pursuant to a CTEP-supported clinical trial setting forth the rights and obligations of each party in a collaborative research effort. It further sets out the obligations of investigators and clinical trial sites participating in CTEP-supported studies under a Collaborative Agreement.

CTEP Collaborator for the purposes of this Agreement, means the pharmaceutical entity that provided CTEP or the clinical trial site with the investigational agent(s) for the clinical trial used to generate the clinical or genomic data ("Data").

Data Access Request (DAR): A request submitted to eNCI Data Access Committee for a specific "consent group" specifying the data to which access is sought, the planned research use, and the names of collaborators and the IT Director. The DAR is signed by the Approved User requesting the data and her/his Institutional Signing Official. Requester Collaborators and project team members on a request must be from the same institution or organization.

Data Use Certification Agreement (DUC): This Agreement between the Approved User, the Requester,

and NIH regarding the terms associated with access and use of controlled-access datasets subject to the GDS Policy and the expectations for use of these datasets.

eNCI Data Access Committee (DAC): The Extramural National Cancer Institute (eNCI) Data Access Committee reviews and approves or disapproves all requests from the research community for access to controlled data of genome-wide association studies (GWAS) of cancer and other genotype-phenotype studies for which it is responsible. The eNCI DAC evaluates the request for conformation to NIH policies and procedures including consistency of the proposed research use with data use limitations stipulated by the Submitting Investigators for each study.

Information Technology (IT) Director: An Approved User who is generally a senior IT official of the Requester with the necessary expertise and authority to affirm the IT capacities at the Requester. The IT Director is expected to have the authority and capacity to ensure that the [NIH Security Best Practices for Controlled-Access Data Subject to the NIH GDS Policy](#) and the Requester's IT security requirements and policies are followed by all of the Requester's Approved Users.

Institutional Certification: Certification by the Submitting Institution that delineates, among other items, the appropriate research uses of the data and the uses that are specifically excluded by the relevant informed consent documents. (See <https://osp.od.nih.gov/scientific-sharing/institutional-certifications/>)

Institutional Signing Official: The individual that has institutional authority to legally bind the institution. The label, "Signing Official", is used in conjunction with the NIH eRA Commons and refers to the individual that has institutional authority to legally bind the institution in grants administration matters. The individual fulfilling this role may have any number of titles in the institution, but is typically located in its Office of Sponsored Research or equivalent. The Institutional Signing Official for the Requester reviews DAR applications submitted by PIs and legally binds the Requester to agree to adhere to the terms described in this Agreement. The Institutional Signing Official for the Submitting Institution enters into the Institutional Certification and signs on behalf of the Submitting Investigator who has submitted data.

Private Cloud System (PCS): A cloud infrastructure provisioned for exclusive use by a single organization comprising multiple consumers (e.g., business units). It may be owned, managed, and operated by the Requester, a third party, or some combination of them, and it may exist on or off premises.

Progress Update: Information included with the annual DAR renewal or Project Close-out summarizing the analysis of controlled-access datasets obtained through the DAR and any publications and presentations derived from the work.

Project Close-out: Termination of a research project that used controlled-access data from an NIH-designated data repository (e.g., dbGaP) and confirmation of data destruction when the research is completed and/or discontinued. The Project Close-out process is completed in the dbGaP authorized access system.

Project Renewal: Renewal of an Approved User's access to controlled-access datasets for a prior-approved project.

Requester: The home institution or organization of the Approved User that applies to dbGaP for access to controlled-access data subject to the GDS Policy.

Requester Collaborator: An individual assisting with the Approved User's research project involving controlled-access data subject to the GDS Policy who is not under the direct supervision of the Approved User. Internal collaborators are employees of the Requester and work at the same location/campus as the Approved User. Note that external collaborators, who are not employees of the Requester and/or do not work at the same location as the Approved User are not "Requester Collaborators" and must be independently approved to access controlled-access data subject to the GDS Policy.

Submitting Institution: An organization who submitted a genomic dataset to an NIH-designated data repository (e.g., dbGaP).

CTEP CRADA Collaborator Review Process (July 12, 2017 version)

1. Prior to submitting their Project and Data Access Request to the database of Genotypes and Phenotypes (dbGaP) authorized access system, the Requesting Investigator⁵ must submit a CTEP Notification to NCICTEPpubs@mail.nih.gov. Please see the CTEP Notification E-mail Template below.

The CTEP Notification includes the Requesting Investigator's assurance that they will comply the 4-week review and comment period before submission for publication or presentation of any manuscripts resulting from the use of CTEP data. This is consistent with the Data Use Certification Agreement for the dbGaP dataset.

In addition, the institution, contact information, dbGaP dataset name and accession number, Research Use Statement, and Non-Technical summary contained in the CTEP Notification must match the information provided in the dbGaP Data Access Request.

CTEP will forward the CTEP Notification to the relevant Collaborator for their review. **Any comments CTEP receives within 14 business days of Collaborator's receipt of CTEP Notification will be shared with Requesting Investigator.** These comments are non-binding.

2. Once the CTEP Notification e-mail has been sent, the Requesting Investigator can continue with the dbGaP authorized access process. The Requesting Investigator is not required to wait for acknowledgment of receipt of the CTEP Notification. However, **the Requesting Investigator must include a copy of the sent CTEP Notification e-mail as part of the data access request.**
3. The extramural NCI Data Access Committee (eNCI DAC) will administratively review the Requesting Investigator's dbGaP Data Access Request and confirm that the Research Use Statement and other information in the Data Access Request are the same as what was provided in the CTEP Notification. If the Data Access Request and the CTEP Notification are not consistent, the request will be administrative returned for revision; the Requesting Investigator will be informed of the reason, provided information on how to correct their request, and given the opportunity to resubmit.
4. Once the Data Access Request passes administrative review, it will undergo full eNCI DAC review. **The due date for full DAC review will be no earlier than three (3) weeks after the date that the CTEP Notification e-mail was sent.** The eNCI DAC will conduct its standard review.

⁵ Requesting Investigator: The person who is the listed Principal Investigator for the dbGaP Project and data access request(s).

CTEP Notification E-mail Template

Dear CTEP,

I am applying through the NIH database of Genotypes and Phenotypes (dbGaP) for access to data related to a NCI Cancer Therapy Evaluation Program (CTEP) clinical trial. I understand that this CTEP trial relates to a drug or agents provided by a CTEP Collaborator (e.g. pharmaceutical or biotech company). I agree that I will allow the CTEP Collaborator a 2-week review of the information related to my DAR so they will understand my intended use of the data generated using their proprietary agent(s). **I understand that this CTEP review process takes place concurrently with my dbGaP project review, and that I can submit my dbGaP authorized access request as soon as I send this CTEP Notification. I will submit a copy of this CTEP Notification with my dbGaP access request.**

For this review, I provide the following information from my dbGaP application:

- a. My institution and contact information (full name, street address, phone number, and e-mail address: [Enter information])
- b. dbGaP Dataset name and accession number (phs): [Enter information]
- c. Research Use Statement: [Enter Research Use Statement]
- d. Non-Technical Summary: [Enter Non-Technical Summary]

I understand that:

1. I will receive an acknowledgement of receipt from CTEP of this email.
2. I may or may not receive any feedback from the CTEP Collaborator.
3. If I do receive comments from the CTEP Collaborator, I will seriously consider them, but they are not binding regarding my use of the CTEP data.
4. As specified in the Data Use Certification (DUC) for the dbGaP dataset I am requesting, **any manuscripts resulting from the use of CTEP data will be submitted to CTEP at this email address (NCICTEPpubs@mail.nih.gov) for CTEP to forward to the relevant CTEP Collaborator(s) for a 4-week review and comment period before submission for publication or presentation.** Any comments and suggestions are non-binding unless they relate specifically to the CTEP Collaborator's Intellectual Property rights regarding the dataset.

Signed,

[Requesting Investigator's name]

Addendum to the Data Use Certification Agreement

Modification of Data Security Terms and Best Practices

Effective for all dbGaP Data Access Requests submitted on or after March 23, 2015, Section 6 of the Data Use Certification Agreement is replaced in its entirety by the following:

6. Data Security and Data Release Reporting

The Requester and Approved Users, including the institutional IT Director, acknowledge NIH's expectation that they have reviewed and agree to manage the requested dataset(s) according to the current NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy and the institutional IT security requirements and policies, and that the institution's IT security requirements and policies are sufficient to protect the confidentiality and integrity of the NIH controlled-access data entrusted to the Requester.

If approved by NIH to use cloud computing for the proposed research project, as outlined in the Research and Cloud Computing Use Statements of the Data Access Request, the Requester acknowledges that the IT Director has reviewed and understands the cloud computing guidelines in the NIH Security Best Practices for Controlled-Access Data Subject to the GDS Policy.

Requesters and PIs agree to notify the NCI DAC of any unauthorized data sharing, breaches of data security, or inadvertent data releases that may compromise data confidentiality within 24 hours of when the incident is identified. As permitted by law, notifications should include any known information regarding the incident and a general description of the activities or process in place to define and remediate the situation fully. Within 3 business days of the NCI DAC notification, the Requester, through the PI and the Institutional Signing Official, agree to submit to the NCI Data Access Committee a detailed written report including the date and nature of the event, actions taken or to be taken to remediate the issue(s), and plans or processes developed to prevent further problems, including specific information on timelines anticipated for action.

All notifications and written reports of data security incidents should be sent to:

NCI Data Access Committee URGENT: NCIDAC@mail.nih.gov

GDS mailbox: gds@mail.nih.gov

NIH, or another entity designated by NIH may, as permitted by law, also investigate any data security incident. Approved Users and their associates agree to support such investigations and provide information, within the limits of applicable local, state, and federal laws and regulations. In addition, Requesters and Approved Users agree to work with the NCI and NIH to assure that plans and procedures that are developed to address identified problems are mutually acceptable and consistent with applicable law.