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Not for distribution

Guidelines for data access/transfer and publications for supplementary biomarker assay analyses involving collaboration between the CIMAC-CIDC Network and the Clinical investigators/Sponsors from PACT-supported clinical trials

DRAFT Version September 14, 2018. When final, attach to Research Collaboration Agreements for CIMACs and CIDC, Proposal Intake Forms, and Data Sharing Agreements.

Purpose of this document: The purpose of this document (“Guidelines”) is to explain the requirements for PACT-funded clinical trials working with the CIMAC-CIDC Network. Specific requirements for sample transfer will be captured in the Human Material Transfer Agreement (HMTA).

In the Cancer Immune Monitoring and Analysis Centers and Cancer Immunologic Data Commons (CIMAC-CIDC) Network, CIMACs will perform bioassays on biospecimens from clinical trials. The bioassay data will be transferred from the CIMACs to the CIDC, and certain clinical data elements (described below) will be extracted and transferred from your affiliated Clinical Trial Network/Research Sites or your institution to the CIDC to enable supplementary biomarker assay analyses. CIMACs and the clinical trial investigators will work together collaboratively to conduct supplementary biomarker assay analyses. The goal of the CIMAC-CIDC Network is to identify biomarkers with translational potential for optimizing immunotherapeutic strategies for patients.

This document addresses the following topics:

- Clinical Data transfer to CIMAC-CIDC
- Biomarker data repository and access
- Proposal approval by PACT JSC
- Guidance for authorship of publications involving data deposited into CIDC

Important note regarding biospecimen transfers: Biospecimens should not be transferred to the CIMACs until the following occur:

- The PACT JSC has approved the Research Project.
- The CIMAC-CIDC Human Material Transfer Agreement (HMTA) has been signed.

Definitions:

“Agent” means an investigational drug, biologic, or product proprietary to a PACT Collaborator, that has been made available under an agreement between PACT Collaborator and your Institution or your Clinical Trial Network and used in association with your described clinical investigation.

“Biospecimens” means blood, serum, urine, saliva, other bodily fluid, bone marrow, cells, stool, or tissue samples/specimens collected from Human Subjects under a Protocol. The term “Biospecimen” further includes, without limitation, any tangible material directly or indirectly

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derived from such Biospecimens collected from Human Subjects under a Protocol, such as genes, gene fragments, gene sequences, proteins, protein fragments, protein sequences, DNA, RNA, and any subcellular structure.

“**CIDC**” means the Cancer Immunologic Data Commons, hosted at Dana-Farber Cancer Institute. The CIDC serves the bioinformatics needs of the CIMACs, including providing a centralized data repository, optimization of data collection methodologies suitable for immune-related biomarkers, data integration, and a shared infrastructure for integrative and correlative analysis.

“**CIMACs**” means the four Cancer Immune Monitoring and Analysis Centers, at Dana-Farber Cancer Institute, Stanford University, The University of Texas MD Anderson Cancer Center, and the Icahn School of Medicine at Mount Sinai, who are responsible for providing a wide range of immune assays on specimens from patients enrolled in clinical trials.

“**CIMAC-CIDC Network**” means the network composed of the four CIMACs and the CIDC supported by NCI U24 Cooperative Agreements to provide an infrastructure to support correlative studies in clinical trials involving immunotherapies, including cross-trial analysis. The goal of this research is to identify biomarkers with translational potential for optimizing therapeutic strategies for Human Subjects.

“**Clinical Investigator**” means, in accordance with federal guidelines, an individual who directs the administration or dispensation of Agent to a Human Subject, and who assumes responsibility for studying the Human Subjects under the Protocol, for recording and ensuring the integrity of research data, and for protecting the welfare and safety of Human Subjects, at a Clinical Research Site.

“**Clinical Research Site(s)**” means the site(s) at which the applicable Protocol will be performed.

“**Clinical Trial Network**”: the clinical research sites/networks that oversee the conduct and coordination of a particular clinical trial. These clinical research sites/networks could include either government, publicly, or privately supported networks.

“**Clinical Trial Team**”: Investigators from the clinical trial, such as the trial Principal Investigator (PI), statistician, and translational leaders.

“**CTEP**” means the Cancer Therapy Evaluation Program, of the Division of Cancer Treatment and Diagnosis (DCTD), which is a program within NCI that plans, assesses, and coordinates all aspects of clinical trials, including extramural clinical research programs, internal resources, treatment methods and effectiveness, and compilation and exchange of data. NCI is part of the National Institutes of Health, a component of the US Department of Health and Human Services.

“**Human Subject**” means, in accordance with federal guidelines, a living individual about whom a Clinical Investigator conducting research under the Protocol obtains:

- (a) data through intervention or interaction with the individual; or
- (b) Identifiable Private Information.

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“Identifiable Private Information” or **“IPI”** about a Human Subject means private information from which the identity of the subject is or may be readily ascertained. Federal regulations defining and governing this information include 45 C.F.R. Part 46 and 21 C.F.R. Part 50.

“NCI Collaborator” means a company that made available its Agent(s) for use in association with the NCI/CTEP-approved Protocol(s).

“PACT”: a project developed by a design team of scientists from industry, government, and academics entitled the "Partnership for Accelerating Cancer Therapies (PACT)" for which a research plan has been developed and ratified by the PACT Joint Steering Committee (“PACT JSC”). The PACT Research Plan (“Research Plan”) will leverage recent National Cancer Institute (“NCI”) investments in its CIMAC-CIDC Network to provide a systematic approach to immune and related oncology biomarker investigation in clinical trials by supporting development of standardized biomarkers and assays.

“PACT Policies” are set forth in the Research Plan.

“PACT Collaborator” means a company that made available its Agent(s) for use in association with the PACT-Funded Trial Protocol(s). When PACT-Funded Trial Protocol is also NCI Clinical Trial Network Protocol, the PACT Collaborator will also be an NCI Collaborator.

“PACT Donor” means an organization that has entered or will enter into a separate agreement with the FNIH for funding PACT.

“PACT Funds” means the funds from PACT Donors provided by the FNIH to Institution for the Research to be performed pursuant to the PACT Research Plan.

“PACT-Funded Trial” means a clinical trial that has been selected by the PACT Clinical Trial Selection Working Group and the PACT JSC to have supplementary biomarker analysis supported by PACT Funds.

“PACT JSC” is the PACT Joint Steering Committee, one of the primary governance bodies for PACT, made up of voting members, which include both the NCI and industry partners, whose responsibilities include, but are not limited to, determining how PACT Funds will be allocated, and selecting clinical trials that will have supplementary biomarker analyses by PACT.

“PACT JSC-approved” means that a Research Project or other effort requiring PACT Funds has been reviewed by the PACT JSC and received a majority vote of approval to receive a portion of the PACT Funds.

“PACT Proposal Intake Form” means the *PACT CLINICAL TRIAL SUPPLEMENTARY BIOMARKER ASSAY PROPOSAL INTAKE FORM*. For each clinical trial submitted for PACT Funds consideration, the proposal response submitted in this form is jointly developed by the Clinical Trial Team, PACT Clinical Trial Selection Working Group, and CIMAC. This form

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serves as the basis for 1) internal review by the PACT Clinical Trial Selection Working Group, 2) tracking by the CIMAC-CIDC Network and 3) review by PACT JSC.

“Protocol” means the Institutional Review Board (“IRB”)-approved clinical investigation under which the Human Material was collected, in which an Agent is administered or dispensed to, or is used involving, one or more Human Subjects. It describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The term “Protocol” includes any and all associated documents, including informed consent forms.

“Required Clinical Data Elements” must include, but are not limited to, demographics; pathology and staging; pathology reports; outcome data; toxicity; study treatments; prior therapies; and all variables and endpoints required for the supplemental biomarker analyses described in the PACT JSC-approved Research Project.

“Research Plan”: The document describing the overall scientific aims and governance of PACT, as well as the initial execution guidelines.

“Research Project”: Specific supplemental biomarker studies related to the Protocol described in each PACT Proposal Intake Form submission, which are collaboratively developed by the Supplemental Biomarker Analysis Team. To become a Research Project, the proposal must first be approved by the PACT JSC. That proposal should then become part of the existing Protocol (except for completed trials – i.e., trial is closed, all patients have completed therapy, and trial has met its primary objectives), or a stand-alone Protocol, which must be approved by the IRB before the Protocol is implemented.

“Supplemental Biomarker Analysis Team”: The collaborative team comprised of the Clinical Trial Team, CIMAC investigators, and PACT Clinical Trial Selection Working Group members (as needed) involved in the design and execution of the Research Project.

Guidelines:

1. The work to be performed within the CIMAC-CIDC Network is a collaboration between the Clinical Trial Team and the CIMAC-CIDC Network investigators throughout the translational study process, from protocol design, bioassay selection and supplemental biomarker analyses, to publications.

The senior statistician from the clinical trial will be included among the clinical trial representatives and will collaborate with the CIMAC-CIDC Network statistician on the supplemental biomarker analyses in which the CIMAC-CIDC Network is involved.

2. Data Access, Use, and Sharing:

a. Transfer of Clinical Data to the CIDC:

Use of the CIMAC-CIDC Network resource will require the Clinical Trial Network or Clinical Research Sites to agree to transfer the Required Clinical Data Elements to the CIDC.

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Timing of clinical data transfer to CIDC:

- i. To enable correlation of supplemental biomarker analyses with clinical data, **relevant Required Clinical Data Elements must be transferred to the CIDC before the CIMAC-generated assay results can be made available to the Supplemental Biomarker Analysis Team** (i.e., including the Clinical Trial Team), and before publication.

The extent and timing of the Required Clinical Data Elements transfer may vary depending on the nature of the trial and the biomarker questions (e.g., demographics, pathology, staging, and prior therapy data may be transferred before outcome data are available; interim data may be transferred before locking of trial data if preliminary analyses are desirable).

Transfer of **all** Required Clinical Data Elements will occur upon locking of trial data, unless otherwise agreed.

- ii. As the CIDC matures, informatics tools will be developed to streamline data transfer. However, the lack of such tools at the outset should not interfere with the submission of the clinical data using existing, available, and agreed-upon transfer tools between the clinical investigators/groups and the CIDC.
- iii. Data transferred to the CIDC must be kept confidential and are subject to data use restrictions (described in Section 2.d).

b. Access to CIMAC-generated bioassay data in CIDC for supplemental biomarker analysis with the Clinical Trial Team:

- i. The CIDC will serve as the data repository for CIMAC-generated biomarker data as well as the Required Clinical Data Elements and will provide the informatics platform for the biomarker analysis by the Supplemental Biomarker Analysis Team.
- ii. The Supplemental Biomarker Analysis Team will use the platform provided by the CIDC to perform their correlative analyses. The CIDC may also provide analytical tools for data analysis within the CIDC portal and CIDC cloud infrastructure.
- iii. The Clinical Trial Team may download and use the data from the CIDC, within the restrictions defined below (Section 2.d).

NOTE: CIMACs will not provide assay data directly back to the Clinical Trial Team; rather, bioassay data will be accessible through the CIDC.

c. Data sharing

- i. The CIMAC-CIDC data sharing plans for PACT-Funded Trials will be consistent with the guidelines in the NCI Cancer MoonshotSM Public Access and

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Data Sharing Policy: <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding/public-access-policy>. The Policy applies to all NCI-Supported Cancer MoonshotSM Research Projects with resulting Publications and Underlying Primary Data, to the extent feasible. The requirements of this Policy are in addition to those requirements and expectations specified under other applicable NIH public access and data sharing policies including but not limited to the [NIH Public Access Policy](#), the [NIH Data Sharing Policy](#), and the [Genomic Data Sharing Policy](#). For additional information, see [NIH Sharing Policies and Related Guidance on NIH-Funded Research Resources](#).

- ii. Since most PACT-Funded Trials will use Biospecimens from existing approved clinical trials from other Clinical Trial Networks/Clinical Research Sites, the CIMAC-CIDC data sharing plans must also comply with the existing data release timelines within these existing Protocol agreements between the Clinical Trial Team and the PACT Collaborator.

Specifically, for NCI/CTEP clinical trials, the CIMAC-CIDC Network data sharing plans must also comply with the timelines stipulated in the NCI cooperative agreement terms of award or the NCI-NCI Collaborator agreements. For example, data, such as clinical and bioassay data, residing in the CIDC and generated from a trial supported via NCI cooperative agreements will be embargoed for use restricted to that trial's investigators, CIMAC-CIDC Network investigators, and NCI Collaborator(s) (i.e. the company[ies] that provided the Investigational Agent to CTEP for the clinical trial), until 6 months after the primary outcome of the trial is either published in manuscript form or posted to ClinicalTrials.gov.

For some trials regardless of their initial source, additional embargo time may be needed for studies being used for regulatory filings by PACT Collaborator(s).

- iii. Following any required embargo period, the data access permissions will be changed to allow the data to become more widely available in the CIDC, the controlled-access database being created to house data generated by the PACT Research Projects and CIMAC-CIDC Network. Each requestor wishing to access the data from PACT and/or CIMAC-CIDC Network Research Projects (whether intramural or extramural) will be required to sign NCI's Data Use Agreement prior to receiving the requested data. All such Data Use Agreements will contain provisions providing for manuscript review by the PACT Collaborator (i.e. the company[ies] that provided the Investigational Agent for the clinical trial) as well as the appropriate intellectual property and the data use rights granted to the PACT Collaborator the original clinical trial agreements.

The PACT Collaborator and/or NCI Collaborator will receive a copy of each request for access to these non-publicly available data and be provided an opportunity to provide comments within 4 weeks of receiving the request.

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d. Use of CIMAC bioassay and clinical data

- i. CIMAC-CIDC Network bioassay and clinical data will only be used to perform the supplemental biomarker study described in the PACT JSC-approved Protocol.
- ii. The Supplemental Biomarker Study Analysis Team will access the bioassay data and Required Clinical Data Elements housed within the CIDC. While the data may be downloaded for the purpose of conducting analyses by authorized individuals of the analysis team, these data must be kept secure and confidential and comply with data use restrictions as defined below:
 - The data should not be released to any entity or individual outside the Supplemental Biomarker Study Analysis Team.
 - The data should be used on computers and in locations with adequate security controls, as defined by policies cited in Section 2(c)(i), at all times.
- iii. Following publication of the biomarker data in a manuscript, the CIMAC-CIDC Network investigators may perform additional analyses of their CIMAC-generated data with approval from the relevant Clinical Trial Team(s), NCI, and the PACT JSC, when PACT-Funded Trial data is used. These additional analyses will require submission of a proposal to NCI describing the proposed analyses, for approval by NCI and PACT Collaborator and/or NCI Collaborator.
- iv. Any other analyses, including cross-trial analyses, in addition to those described in the Research Project, that will be publicly disclosed, including via manuscripts and abstracts, will require approval from NCI and relevant PACT Collaborators and/or NCI Collaborators, and will be subject to the same terms as other Research Projects.

e. Intra-network sharing of CIMAC-CIDC Network PACT-Funded Trial data:

Confidential, internal sharing of data across trials among CIMAC-CIDC Network investigators for activities described in the PACT JSC-approved Proposal Intake Forms, or for validation of clinical utility of biomarkers, is permitted; however, CIMAC-CIDC Network investigators understand that no public disclosure (abstract, manuscript, etc.) resulting from such use of the data or from meta-analysis across PACT-Funded Trials, is permitted without the express, written approval from the PACT JSC and the PACT Collaborator.

f. Biomarker data generated by non-CIMAC labs (including diagnostic company data):

For certain trials, non-CIMAC-generated assay data may be transferred to the CIMAC and CIDC and added to the CIMAC-generated data to enhance the supplemental biomarker analyses, depending on the compatibility of the data format and objectives of study projects. In receiving non-CIMAC assay data, the CIMAC would be required to comply with the terms of the agreement associated with the non-CIMAC-generated

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biomarker data (terms of the agreement would be specific to the situation / source of the data).

Non-CIMAC-generated assay data could include prospective or retrospective assay data.

g. Inventions using data generated by use of Biospecimens from a PACT-Funded Trial

All inventions created using data from PACT-Funded supplemental biomarker analyses will adhere to the PACT Intellectual Property Policy ratified with the PACT Research Plan and detailed below.

No PACT partner or other PACT participant, including a CIMAC-CIDC Network grantee, is obligated to contribute pre-existing intellectual property owned or controlled by it (IP) to the PACT. If a PACT partner or other PACT participant chooses to have their pre-existing IP used in the PACT project, the PACT partner will permit such use, with the limitation that such use is solely for the PACT Project only, without charging a fee. Each PACT partner providing pre-existing IP will notify FNIH, the PACT partners via the PACT JSC, and the LCC if the IP is the subject of a pending patent application(s), an issued patent(s), or is copyright protected.

If a PACT partner or other PACT participant elects to contribute pre-existing IP to the Project, each such PACT partner or other PACT participant will notify FNIH, who will notify the PACT JSC NCI, and the CIMAC-CIDC Network of pending patent applications or issued patents, which the PACT partner owns or has a license to, that may impair the access and free use of PACT de-identified data sets and PACT-Funded Trial results in the CIDC by the general research community as soon as such PACT partner becomes aware of such pending patent application or issued patent.

PACT partners and CIMAC-CIDC Network grantees agree not to file a patent application(s) claiming inventions that are conceived or reduced to practice in the performance of the Research Project using PACT-Funded Trial results that are not publicly available (a "PACT Invention") except in the rare instance when a consensus of FNIH, the PACT JSC and EC agree that it is in the best interests of the goals of the PACT to do so. If, following this consensus, a PACT partner or CIMAC-CIDC Network grantee files a patent application(s) on a PACT Invention such PACT partner or CIMAC-CIDC Network grantee shall grant the PACT partners and all CIMAC-CIDC Network grantees a fully paid up, royalty free, perpetual, irrevocable, non-exclusive license, without possibility to sub-license, to manufacture, make, have made, produce, reproduce, copy, and use the PACT Invention for their own internal research purposes or for submission to a regulatory authority when seeking marketing authorization of the PACT Invention, and/or on a product insert or other promotional material regarding the PACT Invention after having obtained marketing authorization from a regulatory authority.

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The permitted access and use of biospecimens and data created during the PACT project are addressed under the PACT Data Use and Sharing Policies and in more detail in the preceding sections of this document.

As noted in the PACT Data Use and Sharing Policies, all pre-existing CRADA and/or collaborative clinical trial agreements for use of trial data will be honored ahead of this PACT IP Policy. One example of this would be a NCI/CTEP-sponsored clinical trial that also becomes a PACT-Funded Trial will honor existing NCI/CTEP collaborative agreements as articulated in the next section.

h. Inventions using data generated by use of Biospecimens from an NCI/CTEP-sponsored clinical trial

We encourage a responsible approach to management of intellectual property derived from any downstream discoveries that is consistent with the recommendations of the NIH's Best Practices for the Licensing of Genomic Inventions and the NIH Research Tools Policy.

The management of patent applications in a manner that might restrict use of the joint findings and that could substantially diminish the value and public benefit provided by these resources is discouraged. However, if the biospecimens proposed for study are from a clinical trial that was conducted under a binding collaborative agreement with NCI or a pharmaceutical company (for example, with a company that supplied the drug), data sharing may have to await the timelines stipulated in those agreements. Studies conducted under a NCI/CTEP IND are subject to the terms of the CTEP Intellectual Property (IP) Option (http://ctep.cancer.gov/industryCollaborations2/guidelines_for_collaboration.htm) as well as the terms of the CTEP Collaborative Agreement under which the study is conducted. Similarly, studies conducted under a NCTN Group or Company IND will also be subject to the terms of the agreement between the Collaborators which include the CTEP IP Option to Collaborator. Any discoveries from research performed on such specimens will be subject to the CTEP IP Option and/or the licensing terms as required by these agreements.

For avoidance of doubt, a Collaborator who has rights to an invention under the scope of the CTEP IP Option also has the right (a commercial non-exclusive, royalty-free license) to use any data generated in such studies for regulatory filings related to the Agent as well.

3. Publication guidelines:

- a.** All manuscripts, abstracts, or posters using data and/or materials from clinical trials using Agent(s) provided by PACT Collaborator(s), will be sent to FNIH, c/o Stacey Adam at sadam@fnih.org and Jenny Peterson-Klaus at jpeterson-klaus@fnih.org for advisory review and comment by the PACT JSC and the PACT Collaborator no later than thirty (30) days before submission for proposed manuscripts and seven (7) days before disclosure for proposed abstracts or presentations. The PACT Collaborator shall have the right to request that publication be delayed for up to an additional 30 days in

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order to ensure that the PACT Collaborator's confidential and proprietary data, in addition to the PACT Collaborator(s)'s intellectual property rights, are protected.

In all oral presentations or written publications, the PACT team and the PACT Collaborator will be acknowledged unless requested otherwise. Acknowledgement language for the PACT team will be provided to each Supplemental Biomarker Analysis Team. Press releases and other media presentations must also be forwarded to FNIH prior to release.

Note: PACT Collaborator comments are not binding, except that information proprietary to the PACT Collaborator may be redacted.

b. Authorship:

Supplemental biomarker studies using the CIMAC-CIDC Network resources are collaborative efforts between the CIMAC-CIDC Network and the Clinical Trial Teams. **All publications based on CIMAC-CIDC-generated data should recognize this collaboration, through authorship, consistent with general authorship guidelines for collaborative work.**

While a given project may have specific arrangements regarding authorship, some general guidelines can be considered, as follows:

- i. **Manuscript/abstract on primary clinical outcome in which CIMAC-CIDC Network work involves supplemental biomarkers:** Generally, if ancillary biomarker endpoints are included in the primary manuscript for the clinical outcome, the PIs leading the trial (and the statistician analyzing the trial) will have the lead authorship roles. CIMAC-CIDC Network investigators will be included as co-authors or co-lead-authors depending on their specific collaboration in accordance to the level of contribution to the research.
- ii. **Non-primary-outcome manuscripts/abstracts of the trial in which CIMAC-CIDC Network work generates the main findings:** For secondary abstracts/manuscripts that report primarily correlative results, it may be appropriate that CIMAC-CIDC Network lead investigators/statisticians have the lead or co-lead authorship roles. However, each situation is unique and will have to be agreed upon by all of those collaborating in the study.
- iii. **CIMAC-CIDC Network-initiated cross-trial analysis (i.e., across multiple trials):** Depending on the primary purpose of the cross-trial efforts, the Clinical Trial Team(s) and CIMAC-CIDC Network will have to come to agreement on authorship roles. Clinical and CIMAC-CIDC Network investigators will be included in accordance with their level of contribution to the research.