

**For Internal Purposes Only:**

Proposal Version Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Assigned CTWG member:\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

# **Partnership for Accelerating Cancer Therapies (PACT)**

# **Supplementary Biomarker Analysis Proposal**

**Clinical Trial Number:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Trial Name:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Lead PI:** \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Key points about working with PACT and the CIMAC-CIDC Network:**

* The goal of PACT and the Cancer Immune Monitoring and Analysis Centers and Cancer Immunologic Data Commons (CIMAC-CIDC) Network is to identify biomarkers with translational potential for optimizing immunotherapeutic strategies for cancer patients.
* The CIMACs will perform bioassays on biospecimens from the clinical trial and send the bioassay data to the CIDC to enable the correlative analyses.
* As part of the collaboration, the clinical trial group will send required clinical data to the CIDC at the time of supplementary analysis, to enable the correlative analysis. Subsequently, the clinical trial group will send additional clinical data following clinical trial database lock or trial completion, to further annotate the CIDC data. Such additional clinical data would include data on demographics, pathology and staging, outcomes, toxicity, study treatments, prior molecular data (if captured), and prior therapies (if captured) not already sent to CIDC.
* The CIDC will provide the access/platform to investigators to perform the supplementary analysis.
* The supplementary analysis of the bioassays is a collaboration between the clinical trial investigators, the CIMACs, and PACT representatives.
* Following an embargo period, the data will become available for controlled-access data sharing.
* The NCI CTEP IP option applies to all PACT-CIMAC-CIDC projects: <http://ctep.cancer.gov/industryCollaborations2/guidelines_for_collaboration.htm>

**PACT Trial Submission Requirements**

*All submissions must contain the following documentation/information:*

* Clinical trial team has completed all sections of the PACT Intake Form
* Clinical trial team has discussed any existing publication timeline restrictions included in the existing clinical trial agreement with FNIH
* Clinical trial team has ensured that Intellectual Property agreements for the trial proposed are compatible with the CTEP IP Option for Collaborators and the PACT Guidelines
* Current Trial Informed Consent Form has been attached to the Intake Form Packet
* Consent Checklist – The Patient Informed Consent forms for your trial must contain the following items (*sample consent language can be provided upon request*):
	+ Data Sharing consent is compatible with PACT Policies and PACT Guidelines
	+ Data Sharing consent allows for the data to be banked in a controlled online repository for public access for broader research purposes by approved researchers
	+ Safety Event Reporting language assures that the proposed trial was conducted in a safe manner and all appropriate data has been reported to the appropriate regulatory agencies
	+ Sample Collection and Storage consent allows samples to be stored in an appropriately compliant biobank for PACT desired amount of time (recommendation would be at least 15 years)
	+ Sample/Biomarker Testing consent allows samples to be run on any assay
	+ Patients/samples are from the U.S. (currently a requirement until international data rules are dealt with appropriately)
	+ Information detailing that no data from the additional biomarker testing will be returned to treating physicians, patients, or their families

 **Please submit your completed Intake Form to: PACT@fnih.org**

# **PACT Supplementary Biomarker Assay Proposal Intake Form**

## **Section A: Administrative Information**

### **Date of Submission:**

### **Proposal Version:**

### **Clinical Trial Number:**

### **Study Type:**

[ ]Retrospective\*[ ] Prospective

*\*If samples have already been collected for this trial, Section E must be completed*

### **New Submission or Revision:**

[ ]New Submission[ ] Revision to Previous Submission

### **Clinical Trial Team:**

*List the proposal’s clinical trial team, including the clinical trial lead PI(s), translational scientist, and statistician associated with the biomarker studies of the trial.*

|  |  |  |
| --- | --- | --- |
| **Role** | **Name** | **Email address** |
| **Clinical Trial Team** |
| Trial Principal Investigator |  |  |
| Trial Translational Scientist or Correlative Studies Chair |  |  |
| Statistician(s) |  |  |
| Coordination/Operations staff |  |  |
| **Lead CIMAC Team (if known)** |
| CIMAC Principal Investigator |  |  |
| CIMAC Clinician |  |  |
| CIMAC Statistician |  |  |
| CIMAC Project Manager |  |  |

## **Section B: Clinical Trial Objectives, Schema, and Information**

### **Clinical Trial Information:**

Please attach any additional supporting documentation (i.e. research posters, clinical summary reports, public presentations, etc.) that may assist reviewers during the initial stages of the approval process to this intake packet. Documents can be attached either physically or electronically (through a website URL).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Trial Number** | **Trial Title** | **Target Accrual** | **Actual Accrual as of (DATE)** | **Grant/Affiliated Trial Network** *(if applicable)* | **Corporate****Sponsor** *(if applicable)* | **Biobank/Biospecimen storage/collection sites** *(Required)* |
|  |  |  |  |  |  |  |
| **ClinicalTrials.gov Link (if available):**  |

Table 1. Trial Information

### **Trial status (please check one):**

 [ ]In Development [ ]Active/Recruiting [ ]Closed to accrual [ ]Complete

### **Clinical Trial Objectives, Endpoints, and Schema**

1. Primary objectives and endpoints of trial:
2. Trial schema diagram (please indicate timepoints of specimen collections in the schema):

## **Section C: Biomarker Plan**

### **Biospecimen Collection Table**

The purpose of this table/section is to get a better idea of the types of samples your study is collecting and at what timepoints they are being collected. This information should be pulled directly from your study protocol. Please complete the below table with the specimen that you are collecting at each individual timepoint. Please **adapt this table** according to the needs of your trial. Feel free to add any non-PACT assays if applicable (and **delete** example rows that do not apply to your trial).

Ensure that the following table reflects the **most up-to-date** version of your trial’s proposed specimen collection. Please review the most recent specimen umbrella protocol (Appendix E) for the current recommended/required collection protocol. If your collection protocol differs, please call that into account.

| **Specimen Type** | **Archival** | **Baseline** | **[Click and enter Time Point]** | **[Click and enter Time Point]** | **End of therapy** |
| --- | --- | --- | --- | --- | --- |
| **Archival Specimens** |
| **EXAMPLE ROW**FFPE  | 10 Unstained slides;H&E slide | N/A | N/A | N/A | N/A |
| [add rows as needed] |  |  |  |  |  |
| **Core Biopsy Specimens** |
| **EXAMPLE ROW**Cores for FFPE | N/A | Core biopsies #1 and #3 |  |  | Core biopsies #1 and #3 |
| [add rows as needed] | N/A |  |  |  |  |
| **Blood Specimens** |
| **EXAMPLE ROW**Sodium Heparin Green-Top Tubes | N/A | 3 tubes x 10 mL | 3 tubes x 10 mL | 3 tubes x 10 mL | 3 tubes x 10 mL |
| [add rows as needed] | N/A |  |  |  |  |
|  **Other Specimens (for example, stool, bone marrow aspirate)** |
| **EXAMPLE ROW**Stool sample | N/A | OMNIgene GUT kits (OMR-200.100)andALPCO Diagnostics EasySampler Stool Collection Kit | OMNIgene GUT kits (OMR-200.100) | OMNIgene GUT kits (OMR-200.100) | OMNIgene GUT kits (OMR-200.100) |
| [add rows as needed] | N/A |  |  |  |  |

### **Biomarker Plan Table**

The purpose of this table/section is to get a better idea of the types of assays you would like to run on the samples listed in Biospecimen Collection Table 8. Please complete the below table with the assays that you intend to run and explain the purpose of each assay and their corresponding timepoints.

Please **adapt this table** according to the needs of your trial, including adding non-CIMAC or other CIMAC assays. Please ensure the table reflects the **most up-to-date** version of your trial’s proposed biomarker plan.

Please ensure information **is consistent** between the Specimen Collection Table and Biomarkers Table.

**IMPORTANT NOTES:**

* Please limit your timepoints to only 4 timepoints for a given assay.
* For genomic studies, use of flash frozen cores is preferred over use of FFPE cores.
* If flash frozen cores are not obtained, WES and RNA-Seq (or Nanostring) could be prioritized for the FFPE cores.
* **Please indicate, in your protocol**, if tissue cores are to be embedded at the collection site or shipped to the biorepository in 70% Ethanol for processing.

| **Priority** | **Biomarker Name**  | **Assay****(CLIA: Y/N)** | **Use in the Trial** (Integral, Integrated, or Exploratory\*\*) **AND Purpose\*\*\***  | **Specimens Tested** | **Total # of Time points** | **Collection Time Points** | **Mandatory or Optional (M/O) specimen\*\*\*\*** | **Funding Source(s) \*specify if different than PACT\*** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Archival tissue** (re-start Priority # under each tissue-type heading) |
| [#] | **EXAMPLE ROW**PD-L1 [clone]\* | Singleplex IHCCLIA: Y | * Integrated
* Identify biomarkers of response
 | Archival block | 1 | * Archival
 | [specify] | PACT |
|  | [add rows as needed] |  |  |  |  |  |  |  |
| **Tissue-based Biomarkers** (re-start Priority # under each tissue-type heading) |
| [#] | **EXAMPLE ROW**PD-L1 [clone] | Singleplex IHCCLIA: Y | * Integrated
* Identify biomarkers of response
 | FFPE core biopsy | 2 | * Baseline
* End of Therapy
 | M at Baseline | PACT |
|  | [add rows as needed] |  |  |  |  |  |  |  |
| **Blood-based Biomarkers** (re-start Priority # under each tissue-type heading) |
| [#] | **EXAMPLE ROW** [biomarkers] | CyTOFCLIA: N | * Exploratory
* Identify biomarkers of response
 | PBMCs from green-top tubes | 4 | * Baseline
* Day [#] of Cycle [#]
* Day [#] of Cycle [#]
* End of Therapy
 | M | PACT |
|  | [add rows as needed] |  |  |  |  |  |  |  |
| **Other specimens (for example, stool, bone marrow aspirate)** (re-start Priority # under each tissue-type heading) |
| [#] | **EXAMPLE ROW** [biomarkers] | Microbiome (16s)CLIA: N | * Exploratory
* Identify biomarkers of response
 | Stool | 1 | * Baseline
 | O | PACT |
|  | [add rows as needed] |  |  |  |  |  |  |  |

**\* PD-L1 IHC** should be performed using an FDA-approved kit appropriate to the agent (for example, 22C3, 28-8, etc.)

**\*\* Integrated** biomarker studies are defined as assays/tests that are clearly identified as part of the clinical trial from the outset, should be hypothesis-driven, and are intended to address the highest priority scientific questions in the trial. Integrated studies in general should be performed on all trial participants or on a pre-defined subset such as an expansion cohort. **Integral** biomarker analyses are those that must be performed for the trial to proceed – for example, to determine eligibility, to assign treatment or stratify randomization, etc. All other biomarker tests are considered **Exploratory**.

**\*\*\*** **Purpose:** Please **succinctly** state the Purpose/role of the assay (e.g., “hypothesis generation”, “to identify biomarkers of response”, “eligibility criterion”, “assignment to treatment”, “stratification factor”, “response assessment”, “prospective research”, etc.). The full hypothesis should not be included here, but rather below in the section for hypotheses.

**\*\*\*\*Mandatory biopsies** (i.e., biopsy material required for trial participation) must be justified by integral or integrated biomarkers or taken at a timepoint where tissue is also taken for integrated/integral markers.

### **Justification for Selection of Assays**

*Please provide justification and reasoning for the assays requested for PACT funding in the context of the clinical trial, including providing preliminary data if available. For Exploratory biomarkers/assays (Tier 2-3), please provide the scientific rationale for use in this trial.*

### **Objectives and Scientific Hypotheses for Biomarker Plan**

*Please provide the objectives and scientific hypotheses for this PACT biomarker study. Where applicable, please note key markers or marker types to be interrogated by the assay.*

## **Section D: Biomarker Statistical Plan**

*Please refer to Appendix A for additional details on the completion of this section.*

### **Sample size(s) and Rationale:**

### **Case or cohort selection (if applicable):**

**Number of cases:** *How many cases will be included in your PACT biomarker study? (include cohort sizes if cohorts will be studied):*

### **Statistical analysis plan for biomarker analysis:**

## **Section E: Specimen inventory for trials with specimen collections (if applicable)**

If the trial has already completed its specimen collection, please attach an inventory report from the biorepository or trial group’s translational office that contains the following information or complete the table below. Proposals cannot be accepted until a complete list of all available specimens has been provided.

* Specimen type and format
* Timepoint of specimen collection
* Number of cases (patients) with specimens **available for PACT** at this timepoint
* Quantity of specimens **available for PACT** at this timepoint

|  |  |  |  |
| --- | --- | --- | --- |
| Protocol #: \_\_\_\_\_\_\_\_ | **Cohort/Arm 1 (# of cases)** | **Cohort/Arm 2 (# of cases)** | **Total** |
| Archival | Pre-treatment | On-treatment | Post-treatment | Archival | Pre-treatment | On-treatment | Post-treatment |
| **Tissue specimens** |
| FFPE Tissue |  |  |  |  |  |  |  |  |  |
| Frozen Tissue |  |  |  |  |  |  |  |  |  |
| **Blood specimens** |
| PBMCs |  |  |  |  |  |  |  |  |  |
| Plasma |  |  |  |  |  |  |  |  |  |
| Streck tubes |  |  |  |  |  |  |  |  |  |

## **Section G: Signatures**

(This signature page to be completed following approval by PACT.)

**When this PACT proposal has been approved the all parties, a final signed copy will need to be submitted to** **PACT@fnih.org** **for recordkeeping purposes.**

As the clinical trial principal investigator, I acknowledge that my research projects using biospecimens from PACT-funded clinical trials are subject to the requirements in PACT policies for data sharing and public access to publications and to any applicable requirements of collaborative agreements. I understand that, prior to receiving any data or submitting any biospecimens for analysis, my institution will be required to execute a PACT Human Material Transfer Agreement (HMTA) that complies with the PACT Guidelines, which details the requirements for data and biospecimen transfer and use.

**As an investigator on this supplemental biomarker analysis proposal,** I agree to undertake this collaboration, in accordance with the terms above.

**Clinical Trial Principal Investigator** **Name** *(if applicable):* [Single-click here to add text]

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (You may electronically sign.)

Date: [Single-click here to add text]

**If NCTN or Consortia trials, Group Chair or Designee Name:** [Single-click here to add text]

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (You may electronically sign.)

Date: [Single-click here to add text]

Once Approved:

**Lead CIMAC Principal Investigator Name:** [Single-click here to add text]

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (You may electronically sign.)

Date: [Single-click here to add text]

**PACT/FNIH Representative Name:** [Single-click here to add text]

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (You may electronically sign.)

Date: [Single-click here to add text]

## **Section H: References**

### Please provide your references here.

## **Section I: Appendices and Attachments**

### **Appendices**

1. Additional guidance for completing Section D, “Biomarker Statistical Plan”
2. Current Tier 1 and Tier 2 Assay List
3. PACT Policies
4. *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* (“PACT Guidelines”)
5. *Specimen Collection and Processing by Collection Site and Biorepository for CIMAC Studies* (“Umbrella Protocol”)