



Frederick

<b>A. RFP NUMBER:</b> S13-088		<b>B. DATE ISSUED:</b> January 15, 2013	
<b>C. ISSUED BY:</b>		<b>D. ADDRESS OFFERS TO:</b>	
SAIC-Frederick, Inc. Research Contracts Dept. P.O. Box B Frederick, MD 21702		<b>D.1. HARD COPIES (if required):</b>	<b>D.2. ELECTRONIC COPIES:</b>  <a href="mailto:Shaneeka.owens-bearden@nih.gov">Shaneeka.owens-bearden@nih.gov</a>
<b>E. FOR INFORMATION REGARDING THIS SOLICITATION CONTACT:</b>			
<b>E.1. NAME:</b> Shaneeka Owens		<b>E.2. EMAIL:</b> <a href="mailto:Shaneeka.owens-bearden@nih.gov">Shaneeka.owens-bearden@nih.gov</a>	
<b>IMPORTANT:</b>			
<p><b>F.</b> To be considered for award, Offers must be received at the location specified in Block D.2. above by <b>2:00PM EST (EASTERN) on TUESDAY FEBRUARY 26<sup>th</sup>, 2013</b>. Offers must be clearly identified with the solicitation number provided in Block A above.</p>			

### **G. Introduction**

This solicitation is issued by SAIC-Frederick, Inc. (SAIC-F), a wholly owned subsidiary of Science Applications International Corporation under its prime contract with the Frederick National Laboratory for Cancer Research (FNLCR) in Frederick. The provisions and clauses contained herein and attached are influenced by and reflect the relationship of the parties in that Agreement, which was awarded and is administered under the provision of the Federal Acquisition Regulation (FAR).

### **H. Request for Proposal (RFP) Package**

This RFP package consists of two documents: this one, which is referred to as the RFP Document, and another, which is referred to as the Agreement Document. The Agreement Document is being provided in advance of award, so that the Offeror may review SAIC-F Terms and Conditions. A final Agreement Document will be issued at time of Award.

### **I. Agreement Type/Procurement Objective**

It is anticipated that this RFP will solicit proposals from qualified potential sources in response to the technical challenges and objectives described herein and attached. The resulting Agreement will be a hybrid combination of multiple agreement types. Firm-Fixed pricing will be utilized for milestone payments associated with Institutional Review Board (IRB) approval and executing a Material Transfer Agreement (MTA). Fixed-Unit pricing shall apply to the delivery of tumor samples, case reports/diagnostic histopathology and one-year case reports respectively. A Firm-Fixed and/or Fixed-Unit Price Agreement provides for a price that is not subject to any adjustment as a result of the Subcontractor’s cost experience. The Subcontractor may not exceed the established fixed amount without the prior approval of the Contracting Officer.

For Travel Expenses **ONLY** the resulting Agreement will be Cost Reimbursable as described in FAR Part 16.302. A Cost-Reimbursement Agreement provides for payment of allowable incurred costs to the extent prescribed in the Agreement. The Subcontractor may not exceed the established ceiling amount without the prior approval of the Contracting Officer.

## **J. Instructions to Offerors**

### ***J.1. General Information***

IMPORTANT:

PROPOSALS MUST BE SUBMITTED ELECTRONICALLY IN EITHER SEARCHABLE ADOBE ACROBAT, MICROSOFT WORD, OR MICROSOFT EXCEL FORMATS AS APPLICABLE. SAVED FILES MUST NOT EXCEED 15 MB IN SIZE; THIS MAY REQUIRE THAT A DOCUMENT BE BROKEN INTO TWO OR MORE SEPARATE FILES.

ALL OFFERS MUST BE RECEIVED BY **2:00PM EST (EASTERN) ON TUESDAY FEBRUARY 26<sup>TH</sup>, 2013**. Proposals shall be submitted to Shaneeka Owens at [Shaneeka.owens-bearden@nih.gov](mailto:Shaneeka.owens-bearden@nih.gov).

All submissions must be clearly identified to include the Offeror's name, Principal Investigator's name (or Project Manager's name), and RFP number.

Late offers will not be considered for award.

#### **J.1.a. Conflicts of Interest**

"Offerors who have a potential Conflict of Interest must notify SAIC-F in writing and provide a mitigation plan addressing the conflict **at least 2 weeks prior to the submittal due date for proposals**.

If this direction is not followed, Offeror will be disqualified from the competition."

### ***J.2. Questions Regarding This Solicitation***

IMPORTANT:

ALL QUESTIONS OR REQUESTS FOR CLARIFICATION MUST BE EMAILED TO SHANEEKA OWENS AT [Shaneeka.owens-bearden@nih.gov](mailto:Shaneeka.owens-bearden@nih.gov) NO LATER THAN **2:00PM EST (EASTERN) on THURSDAY JANUARY 31<sup>st</sup>, 2013**. Questions shall be provided in one concise submission with references to the relevant sections(s) of the RFP. The questions submitted will be compiled with responses into one document that will be incorporated as an amendment to this RFP and distributed to Offerors.

Questions or requests directed to any other individual other than the individual named in this section will not be considered valid, nor will there be a response provided. If deemed necessary or desired by the SAIC-F Contracting Officer, a second round of questions may be solicited.

### ***J.3. Bidders' Teleconference***

#### **IMPORTANT:**

A PREPROPOSAL TELECONFERENCE WILL BE HELD ON **THURSDAY FEBRUARY 7<sup>th</sup>, 2013 AT 12:00PM EST (EASTERN)**. This call will provide Offerors the opportunity to ask additional questions and receive answers in a "live" venue. Offerors wishing to participate in this teleconference shall dial 1-800-366-7242 and enter passcode 1375607 when prompted. Individuals calling in from outside the United States may dial 1-858-826-6707 and enter passcode 1375607 when prompted.

### ***J.4. RESERVED***

### ***J.5. Proposal Instructions to Offeror***

To be considered responsive to this RFP, the Offeror must provide and/or complete the following requirements:

#### **J.5.a. VOLUME 1 – RFP**

This document shall contain the RFP Document with all items completed as required below and submitted as prescribed in J.1. General Information above. The document shall be clearly named Volume 1 – RFP.

Requirements:

Complete Section L. Representations and Certifications of this document.

Complete Section M.1. Subcontracting Certification of this document and, if applicable, provide a subcontracting plan as described in FAR 19.704. A subcontracting plan template may be found at <http://www.hhs.gov/osdbu/SubcontractPlan-FY08.doc>.

Complete Section M.2. E-Verify Compliance

Complete Section N. Offeror Representatives identifying the (1) Official Authorized to Negotiate on behalf of Offeror, (2) Offeror Key Personnel, (3) Offeror Invoice Representative, (4) Offeror Invoice Remittance Address, and (5) Offeror Regulatory Affairs Representative.

Complete Section O. Offeror Signature designating the individual duly authorized to make an Offer on behalf of the Offeror.

Complete and submit with the offer an IRS Form W-9. All Offerors MUST be registered with the System for Award Management (SAM) -- formerly the Central Contractor's Registration (CCR). Offerors may register with SAM at

<http://www.sam.gov>. The address included on the W-9 MUST match the address registered at SAM, and/or included with the Representations, Certifications, and Other Statements of Offerors.

Complete RFP Attachment 4 – Certificate of Accounting and Billing System Adequacy.

#### **J.5.b. VOLUME 2 – TECHNICAL PROPOSAL**

This document shall contain the Technical Proposal Document with all items completed as required below and submitted as prescribed in J.1. General Information above. The document shall be clearly named Volume 2 – Technical Proposal.

Requirements:

The Offeror must provide proposals that clearly demonstrate the Offeror's current capabilities to meet each of the various requirements as established in RFP Attachment 1 – Statement of Work and in accordance with the guidelines set forth in RFP Attachment 2 – Technical Proposal Information Requirements. Responses shall be focused, succinct, and free of extraneous data or information responding solely to the requirements contained in this RFP. Additionally, technical proposals shall be formatted in such a way to clearly cross-reference the relevant sections in the RFP.

#### **IMPORTANT:**

Technical proposals shall not include cost or pricing information.

Technical Proposals must include page numbers on all pages, including all appendices and attachments. There must also be a cover page that lists all appendices and attachments.

Please refer to RFP Attachment 2 – Technical Proposal Information Requirements for an outline of specific information to be addressed in the Technical Proposal and for maximum page limitations for each of the required sections.

#### **J.5.c. VOLUME 3 – COST (OR PRICE) PROPOSAL**

This document shall contain the Cost (or Price) Proposal Document with all items completed as required below and submitted as prescribed in J.1. General Information above. The document shall be clearly named Volume 3 – Cost (or Price) Proposal.

Requirements:

Offerors shall submit Cost (or Price) Proposals that provide a cost for the project proposed. The Cost (or Price) Proposal shall include the information required in RFP Attachment 3 – Cost (or Price) Proposal Information Requirements. Cost proposals provided in response to this RFP will be used for planning and evaluation purposes. Any

requests from Offerors to revise the original cost proposal, as the result of changes requested to the original technical approach during subcontract negotiations, may be considered but these requests from Offerors must be accompanied by a detailed explanation of the nature and impact of the change and the need for monetary adjustment.

**Travel:**

Funds may be requested to cover the cost of one trip to attend the CPTAC Program annual meeting.

***J.6. RFP Point of Contact***

The Point of Contact for this RFP is identified below.

Name: Shaneeka Owens  
 Address: SAIC-Frederick, Inc.  
 P.O. Box B  
 1050 Boyles Street, Fort Detrick  
 Frederick, MD 21702-1201  
 Email: [Shaneeka.owens-bearden@nih.gov](mailto:Shaneeka.owens-bearden@nih.gov)

***J.7. RFP Attachments***

The following are considered attachments to this RFP:

<b>RFP Attachment No.</b>	<b>Document Description</b>
1	Statement of Work
2	Technical Proposal Information Requirements
3	Cost (or Price) Proposal Information Requirements
4	Certificate of Accounting and Billing System Adequacy

**K. Proposal Evaluation Criteria**

***K.1. Basis for Award***

SAIC-F intends to award an Agreement(s) resulting from this RFP to the responsible organization(s) whose offer(s) conforming to the RFP will be of the best value to SAIC-F, price and other factors considered. Although technical factors are of paramount consideration in the award of an Agreement, cost and/or price is also important to the overall award decision.

## ***K.2. Potential Award Without Discussions***

SAIC-F reserves the right to award an Agreement without discussions if the Contracting Officer determines that the initial offer(s) are fair and reasonable and that discussions are not necessary. Therefore, the Offeror's initial offer should contain the Offeror's best terms from a price and technical standpoint. However, SAIC-F reserves the right to conduct discussions if later determined by the Contracting Officer to be necessary. SAIC-F may reject any or all offers; accept other than the lowest priced offer; and waive informalities and minor irregularities in offers received.

The assessment of the offers received in response to this RFP will be carefully considered against the needs of SAIC-F and the NCI. This assessment is not intended to be a solely mechanical or mathematical analysis of an offer, but rather the product of both objective and subjective measurements and judgments of the source selection officials after consideration of the relevant information.

## ***K.3. Proposal Evaluation Factors***

Evaluation of the offers submitted will be considered against the following evaluation factors.

### **K.3.a. Technical Approach**

The Offeror demonstrates good understanding of the scope, objectives, and challenges of this project.

The proposed approach is consistent with the CPTAC Tissue Procurement Protocol(s) for the tumor type proposed.

The solution proposed is within the scope of the SOW.

Offeror can meet specimen processing and storage requirements.

### **K.3.b. Team and Key Personnel**

Project Organization covers all skills needed to fully execute this project.

Key personnel have demonstrated experience in the technical evaluation factors given above that are applicable to their role.

Evidence has been provided that Key Personnel have performed successfully in the past in the role proposed.

Key personnel are bid at a level of effort commensurate with their proposed role.

### **K.3.c. Experience and Past Performance**

The Offeror has demonstrated experience in the technologies and procedures required to execute this project.

Past performance examples are for projects of similar size, scope, and technical objectives.

Evidence of successful performance on these projects has been provided.

#### **K.3.d. Management**

Project Management Approach is sufficient to meet the objectives in the SOW.

Mechanism by which project, budget and costs are controlled has been described.

Project risks have been identified and risk mitigation strategies have been identified.

Subcontractor roles are defined and management controls are adequate.

Schedule to provide the specimens is reasonable.

#### **K.3.e. Cost Reasonableness**

Costs proposed are commensurate with the technical tasks bid.

### **L. Representations and Certifications**

In order to be considered responsive, all Offers must include a completed and signed set of general Representations, Certifications, and Other Statements of Offerors (Representations and Certifications). Offerors must access <http://rcb.cancer.gov/rcb-internet/forms/rcneg.pdf> to complete their Representations and Certifications. **Offeror shall note that Representations and Certifications generated through ORCA will not be accepted.**

- Our organization's DUNS Number is Insert DUNS Number.
- Our organization certifies that it has Insert # of Employees employees.

### **M. Certifications**

#### ***M.1. Subcontracting Certification***

In accordance with the terms of its prime contract, under which a resulting award will be issued, SAIC-F is committed to maximizing small business subcontracting opportunities to the maximum extent practicable. In pursuit of this objective, please complete and include in your technical proposal the following certification providing the percentage of effort that will be conducted by employee personnel during the execution of the Statement of Work as provided herein (including any option tasks/periods, as applicable):

By submission of this signed offer, Insert Organization Name hereby certifies that \_\_\_\_%\* of the effort expended in the execution of the Statement of Work as provided by SAIC-F in solicitation number Insert RFP Number (Block A Above) will be conducted by employees of this organization.

By:

Title:

Signature:

Date:

\*If the percentage of work to be conducted by employees of your organization is less than 100% and the total cost proposed is \$650,000 or more a small business subcontracting plan as described in FAR 19.704 is required prior to award of an Agreement. Failure to provide an acceptable subcontracting plan in a timely manner may render your organization ineligible for award. A subcontract plan template may be found at <http://www.hhs.gov/osdbu/SubcontractPlan-FY08.doc>.

***M.2. E-Verify Compliance (FAR 52.222-54)***

- Subcontractor is currently enrolled in the DHS E-VERIFY system (Employment Eligibility Verification) Please provide a copy of the Edit Company Profile page as proof of enrollment.
- Subcontractor is currently NOT enrolled in the DHS E-VERIFY system

To be eligible for award Subcontractor will be required to enroll in E-VERIFY within 30 days from date of award and must provide a copy of the Edit Company Profile page. To access E-verify, you may visit <https://e-verify.uscis.gov/enroll>.

**N. Offeror Representatives**

***N.1. Offeror Authorized Representative***

The following individual(s) is/are the designated representative of the Offeror. This will be the Official authorized to negotiate and sign the resulting Agreement:

Name

Title

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Organization

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Address Line 1

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Address Line 2

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City, State, and ZIP Code

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Phone:

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Fax:

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Email:

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***N.2. Offeror Technical Representative(s) and/or Key Personnel***

The following individual(s) is considered to be essential to the work being performed hereunder, and shall not be re-assigned, removed, or substituted without the concurrence of the Contracting Officer:

Name	Title	Email Address

***N.3. Offeror Invoice Representative(s)***

The following individual(s) is the designated representative to submit invoices:

Name

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Title

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Organization

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Address Line 1

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Address Line 2

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City, State, and ZIP Code

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Phone:

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Fax:

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Email:

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**N.3.a. Offeror Invoice Remittance Address**

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Organization

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Address Line 1

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Address Line 2

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City, State, and ZIP Code

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***N.4. Offeror Regulatory Affairs Representative(s)***

The following individual(s) is the designated representative handling all matters pertaining to Regulatory Affairs:

Name

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Title

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Organization

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Address Line 1

---

Address Line 2

---

City, State, and ZIP Code

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Phone:

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Fax:

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Email:

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**O. Offeror Signature**

The following individual is duly authorized to make an Offer on behalf of the Offeror. Offer shall be valid for 90 days.

Offeror certifies by signing this Offer that the Representations and Certifications submitted with this offer have been completed within the last 12 months and that all information contained therein is current, accurate, complete, and applicable to this Offer and shall be hereby incorporated into any resulting Agreement that shall result from this Offer.

Signature

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Name

---

Title

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Organization

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Address Line 1

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Address Line 2

---

City, State, and ZIP Code

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Phone:

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Fax:

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Email:

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## **Attachment 1: Statement of Work**

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## A. Background

Despite significant progress in understanding cancer at the molecular level, the sheer complexity of the over 200 diseases that comprise “cancer” is a daunting barrier to developing the interventions needed to diagnose, treat, and prevent cancer. Vital to the progress in these areas is the discovery and understanding of cancer-specific aberrations at various molecular and cellular levels. Although proteins reflecting the genomic changes in cancer have the potential to become clinically meaningful biomarkers, their discovery and validation has proven to be challenging. As a result, few biomarker candidates have been translated into clinical utility.

Two key barriers in the early stages of biomarker development are: 1) a limited understanding of the changes in cancer genomes that translate into functional differences at the proteomic level; and 2) insufficient technologies that could be widely applied to reproducibly detect and quantify these aberrant proteomic changes across samples from cancer and control populations. Significant barriers to the development of cancer protein biomarkers include insufficient inter-laboratory reproducibility, a lack of standards for proper study design, various analytical barriers, biospecimen collection/handling, data acquisition/analysis, and a notable absence of reference standards and high quality reagents. The progress in the field has also been hampered by the lack of a coherent “pipeline” to connect biomarker discovery with well-established methods for clinical validation. Although various cancer-related proteomic changes have been identified in numerous published studies, these studies mostly came from diverse research groups working independently. Consequently, the findings are typically based on an insufficient number of samples to have adequate statistical power needed for rigorous evaluation of the observed protein changes as specific, clinically relevant cancer biomarkers.

Recognizing this need for an evidence-based, efficient proteomics pipeline, the NCI launched the Clinical Proteomic Technology Assessment for Cancer program (CPTAC) in 2006. At that stage (Phase I), the CPTAC initiative focused on removing the analytical and technical barriers in order to enable the accurate and reproducible identification and quantification of a meaningful number of proteins to drive clinically-relevant biomarker qualification studies. Phase I of the CPTAC program has demonstrated the effectiveness of a multi-disciplinary, multi-institutional approach in addressing long-standing problems of analytical variability in proteomics and exploring ways to overcome the inherent variability of specific analytical platforms in order to uncover and quantify real biological differences.

Although discovery efforts oriented on cancer protein biomarkers identify many hundreds to thousands of candidate biomarkers, CPTAC investigators recognized that only a few would eventually prove clinically useful that can be analytically validated. Therefore, developmental strategies must allow for an efficient testing of many biomarker candidates to identify and verify those few that would be suitable for further clinical implementation. Addressing this need, researchers involved in Phase I of the CPTAC program designed a two-step strategy (further referred to as the developmental “pipeline”) for the efficient, timely, and cost-effective development of protein (and peptide) biomarkers prior to clinical validation studies. The two steps, referred to as “Biomarker Discovery” and “Biomarker Verification”, are outlined below and in Figure 1.

***Biomarker Discovery***

As the first step of the CPTAC-established pipeline, cancer-specific biomarker candidates are discovered (identified) using metrics-driven protein profiling technologies that interrogate appropriate biospecimens (e.g., tumor and proximal fluid). The discovery platforms (based on mass spectrometry and affinity-based capture immunochemistry) have proved to be sufficiently robust to reveal a large number of protein biomarker candidates. These biomarker candidates identified in the Discovery step must then be evaluated in independent biospecimen collections larger than those used initially.

***Biomarker Verification***

Following biomarker discovery, some candidates can be further analyzed (verified) using commercially available reagents (notably, antibodies for immunoassays). However, moving candidates from discovery to clinical validation typically requires overcoming various bottlenecks reflecting a lack of commercially available, high quality affinity reagents (antibodies) in adequate numbers, their high costs, and/or lengthy production times. These limitations are addressed in a comprehensive manner by the Verification step of the CPTAC pipeline. Verification involves the development of targeted, reproducible, quantitative assays, which are commonly multiplexed and thus suitable for the examination of a larger number of biospecimens (e.g., tumor, proximal fluid, blood) to ensure appropriate statistical power. The Verification step and the established assays are meant to be cost effective and timely in terms of funneling those few biomarker candidates for further clinical validation studies. Although CPTAC teams are not involved in large scale clinical validation studies, their verified candidates will the potential to move downstream into clinical testing.

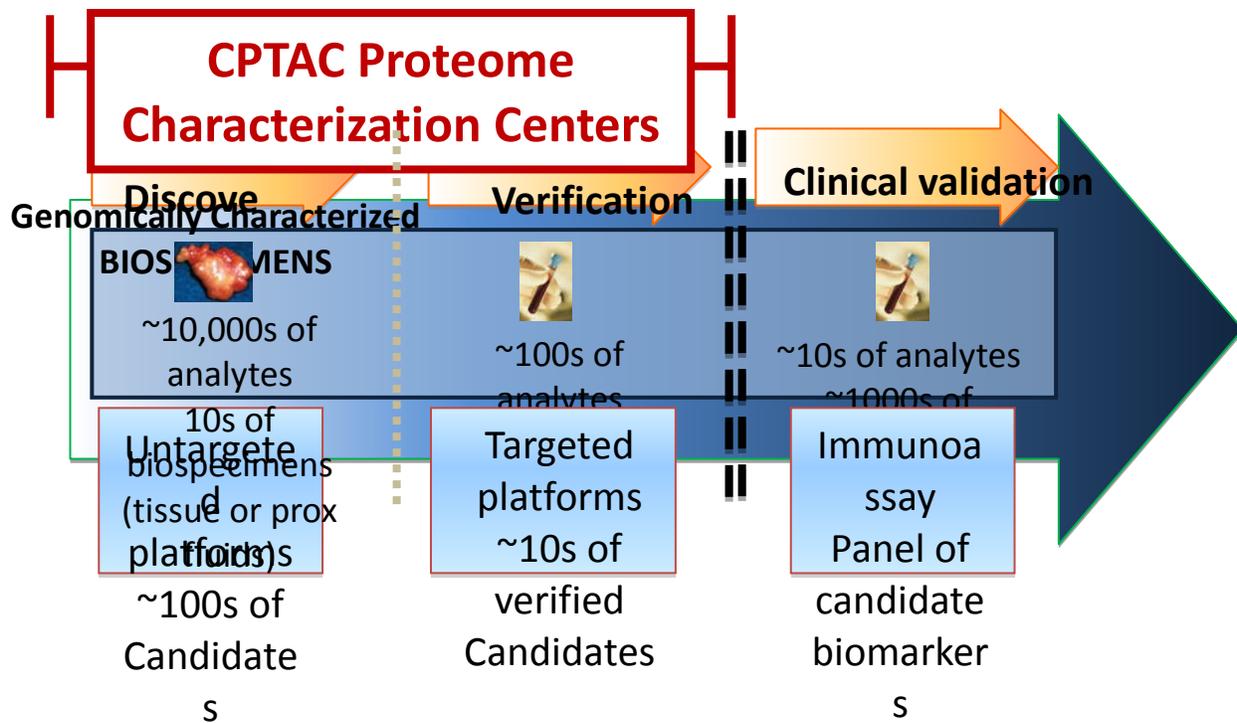


Figure 1: CPTAC Pipeline

Recently, significant progress has been made in characterizing and sequencing the genomic alterations in statistically robust numbers of samples from several types of cancer. For example, The Cancer Genome Atlas (TCGA), International Cancer Genome Consortium (ICGC) and other similar efforts are identifying genomic alterations associated with specific cancers (e.g., copy number aberrations, rearrangements, point mutations, epigenomic changes, etc.). The availability of these multi-dimensional data to the scientific community sets the stage for the development of new molecularly targeted cancer interventions. Understanding the comprehensive functional changes in cancer proteomes arising from genomic alterations and other factors is the next logical step in the development of high-value candidate protein biomarkers. Hence, proteomics can greatly advance the understanding of molecular mechanisms of disease pathology via the analysis of changes in protein expression, their modifications and variations, as well as protein-protein interaction, signaling pathways and networks responsible for cellular functions such as apoptosis and oncogenesis.

Realizing this great potential, the NCI launched the second phase of the CPTC initiative in September 2011. Renamed the Clinical Proteomic Tumor Analysis Consortium, CPTAC is beginning to leverage its analytical outputs from Phase I to define cancer proteomes on genomically-characterized biospecimens. The purpose of this integrative approach is to provide the broad scientific community with knowledge that links genotype to proteotype and ultimately phenotype.

The key programmatic components of CPTAC Phase II include: Tissue Source Sites (TSS); a Biospecimen Core Resource (BCR); Proteome Characterization Centers (PCCs); a CPTAC Steering Committee (SC); a CPTAC Biomarker Candidate Selection Subcommittee (BCSS); a Data Coordinating Center (DCC); and a data portal. Each PCC consists of a discovery unit, verification unit, and administrative core. A schematic representation of the CPTAC project is shown in Figure 2.

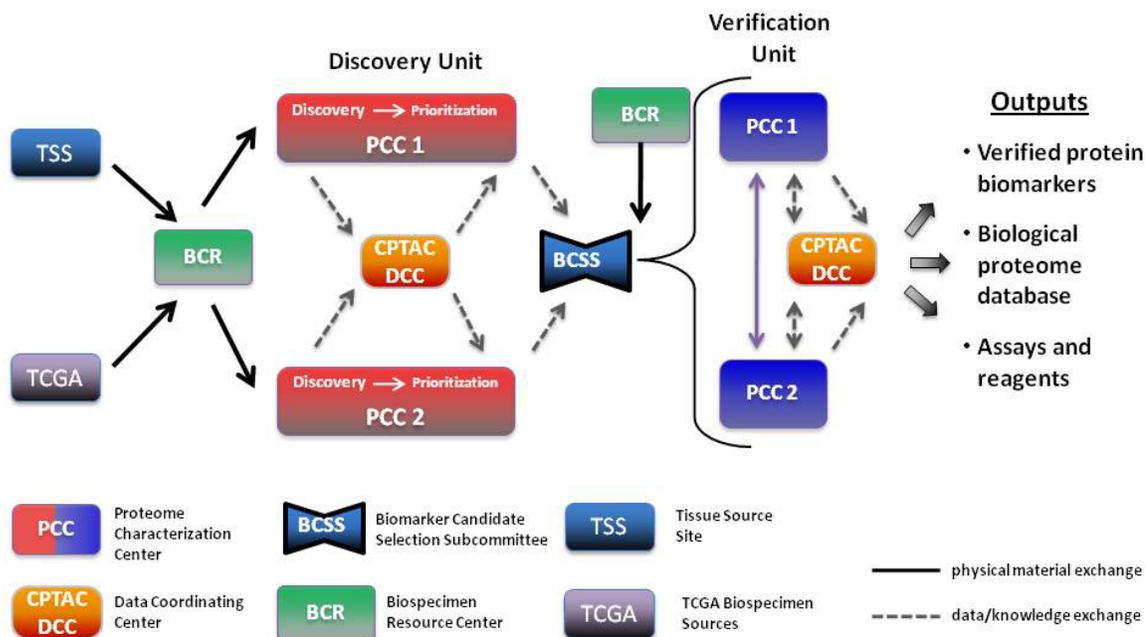


Figure 2: CPTAC Workflow

In Phase I of CPTAC, research centers shared data by depositing data files to a data repository entitled Tranche hosted by the University of Michigan. Since most of these data files were generated in technology assessment and benchmarking experiments, experimental annotation focused on the technical aspects of sample analysis and processing. However, data production Phase II of CPTAC is expected to exceed that of Phase I with the inclusion of experimental annotation of more refined descriptions of the samples involved, as well as de-identified clinical data accompanying each sample. Finally, since many of the samples have or will have undergone genomic analysis, complete data management of CPTAC data files will include connectivity between the proteomic data and genomic data. All data produced is formally hosted by the CPTAC DCC and can be found at <https://cptac-data-portal.georgetown.edu/cptacPublic/>.

## B. Scope

The scope of work under this Statement of Work (SOW) encompasses the activities needed to prospectively procure high quality, clinically annotated human tumor samples and when feasible, normal tissue from volunteer patients suffering from colon, ovarian, and breast cancer. The overall programmatic goal is to procure tumor tissue meeting quality requirements from 100 cases from each cancer type. Collection will stop once those thresholds are met. The tissue will be utilized for CPTAC Program Phase II with the samples obtained under conditions optimized for proteomic analysis. The tissue procurement will be consistent with the CPTAC tissue procurement protocols (attached in Appendix 2). The scope will also encompass obtaining blood and plasma from each case along with the longer-term follow up of the clinical status of patient volunteers are procurement, as well as interacting with the CPTAC Program.

**C. Period of Performance**

The base Period of Performance will be 12 months with one 12-month option. The long-term (i.e., five year) patient follow up noted in the Tissue Procurement Protocols is not within the scope of this SOW and will be addressed at a later date.

**D. Place of Performance**

The work will be performed at the Subcontractor's facilities

**E. Objectives**

At a minimum, this SOW supports the following tasks for all biospecimens and data submitted:

**E.1. Obtaining Institutional Review Board Approval**

E.1.a. The subcontractor shall provide written documentation to the SAIC-Frederick (SAIC-F) Technical Project Manager (TPM) and CPTAC BCR that an Institutional Review Board (IRB) has reviewed and approved participation specifically in the CPTAC program. Such approval includes the cases when an IRB does not consider the work to be human subjects research or considers the work to be exempt; documentation of these IRB positions is still required. This approval must be documented annually and shown to be current, even after the subcontract period ends if additional follow-up data are going to be made available.

E.1.b. The subcontractor shall develop appropriate patient consent documents and have these reviewed and approved by an IRB. This approval must be documented with the SAIC-F TPM and CPTAC BCR.

**E.2. Executing Material Transfer and Data Use Agreements**

The Subcontractor shall develop and obtain any needed local approval for a Material Transfer Agreement (MTA) that contains a Data Use Agreement (DUA) with the CPTAC BCR. The Subcontractor shall enter into the Agreement.

### **E.3. Enrolling Patients**

The subcontractor shall be responsible for recruiting, consenting, and enrolling patient volunteers as approved by the IRB. The Subcontractor shall also be responsible for obtaining clinical data on the volunteers and submitting a de-identified version of that data to the CPTAC BCR via an electronic interface to a clinical data repository. The specific data to be collected will be disease specific and the specific data elements determined at a later date.

### **E.4. Procuring, Processing, and Shipping Tissue and Blood**

The Subcontractor shall obtain tumor and blood samples from consented volunteer patients. When appropriate, the Subcontractor may also obtain normal tissue. The subcontractor shall provide for the short-term storage of the tissue specimens at vapor phase liquid nitrogen temperature and blood at -70°C and adhere to the instructions provided by the BCR for shipping the specimens.

### **E.5. Obtaining Initial Patient and Diagnostic Histopathological Data**

The subcontractor shall be responsible for obtaining initial clinical data on the patient along with pathology reports for the cases submitted to the BCR. The reports shall be de-identified and electronic copies submitted to the BCR as soon as reasonably possible after the tissue has been shipped. The subcontractor shall also be responsible for obtaining high-quality electronic images of the FFPE H&E slides representative of the diagnosis in the pathology report and submit them to the BCR (or provide physical slide(s) that will be returned after imaging). For certain tumors, unstained FFPE slides will be required and submitted to the BCR.

### **E.6. Long-term Patient Follow Up**

The subcontractor shall be responsible for obtaining patient clinical data and status at the start of the initial treatment regimen and at one year after the end of the initial treatment regimen. The Subcontractor shall submit de-identified versions of that data to the CPTAC BCR via an electronic interface to a clinical data repository. The specific data to be collected will be disease specific and the specific data elements determined at a later date. The subcontractor shall also identify any patients that have been lost to follow up.

### **E.7. Interacting with Other Stakeholders**

The subcontractor shall participate in monthly calls amongst SAIC-F, the NCI and other Subcontractors participating in the program. The Subcontractor shall also participate in the CPTAC Annual Meeting.

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**F. Constraints****F.1. Institutional Review Board Approval**

- F.1.a. The IRB protocol shall be based on the information contained in Appendix 3.
- F.1.b. Patients must give informed consent for collection of the cancer and blood samples with genetic and/or genomic research being specifically permitted.
- F.1.c. The subcontractor shall provide assurance of donor-specific date of consent for all cases.
- F.1.d. The subcontractor shall provide the SAIC-F TPM and CPTAC BCR copies of:
  - F.1.d.(1). IRB protocols
  - F.1.d.(2). IRB approvals
  - F.1.d.(3). The current informed consent form

**F.2. Material Transfer Agreement/Data Use Agreement Approval**

- F.2.a. A copy of the executed MTAs, with signatures, shall be provided to the SAIC-F TPM and the CPTAC BCR in advance of any work done under this subcontract.
- F.2.b. Neither the NCI nor SAIC-F shall be a party to the MTA.
- F.2.c. The MTA terms shall include the following:
  - F.2.c.(1). MATERIAL shall be defined to include both the physical biospecimens and the associated annotation data.
  - F.2.c.(2). MATERIAL is for research use only, i.e., not for treatment, transplant, or diagnosis.
  - F.2.c.(3). All parties shall comply with relevant laws.
  - F.2.c.(4). PROVIDER does not retain intellectual property reach through rights to datasets generated with MATERIALS or DERIVATIVES or to future discoveries arising from those datasets.
  - F.2.c.(5). Terms shall not differentiate between nonprofit and for-profit entities being part of CTPAC operations or data generating networks.
  - F.2.c.(6). Terms shall not differentiate between nonprofit and for-profit entity access to datasets.

F.2.c.(7). RECIPIENT is the custodian of the MATERIAL and acquires no ownership or intellectual property rights in the MATERIAL, derivatives, or future discoveries.

F.2.c.(8). At the end of the project, MATERIAL and derivatives shall be disposed of under the direction of NCI.

F.2.c.(9). MTA shall pre-authorize the BCR to redistribute MATERIAL and DERIVATIVES to the various centers associated with CPTAC.

F.2.d. Regarding associated annotation data, MTA terms shall include:

F.2.d.(1). A requirement that incoming data from the subcontractor shall be compliant with HIPAA-defined “Limited Data Set” with the expectation that date/timestamp and geographical data will be included. PROVIDER shall warrant that data are in compliance.

F.2.d.(2). Language for a HIPAA-compliant “Data Use Agreement” shall be included. The data use agreement shall pre-authorize the BCR to further transmit “Limited Data Set” compliant data to CPTAC Data Coordinating Center (DCC) under an appropriate Data Use Agreement (DUA).

F.2.e. MTA shall require that the RECIPIENT not attempt to identify or contact MATERIAL donor or family members.

### F.3. Patient Enrollment

F.3.a. Only patients suffering from breast, ovarian, and colon are eligible for enrollment.

F.3.b. The inclusion and exclusion criteria shall conform to those listed in the respective CPTAC Tissue Procurement Protocols.

### F.4. Procuring, Processing, and Shipping Tissue and Blood

F.4.a. Primary tumor samples:

F.4.a.(1). The procurement of primary tumor samples for each cancer type must conform to the respective Tissue Procurement Protocol contained in Appendix 2.

F.4.a.(2). All tissue samples must be stored at vapor phase liquid nitrogen temperature at the subcontractor’s facility until shipped to the CPTAC BCR.

F.4.b. Blood

- F.4.b.(1). The procurement of plasma and blood cells for genomic analysis must conform to the respective Tissue Procurement Protocol contained in Appendix 4.
- F.4.b.(2). Plasma and red cell pack shall be obtained and processed per Standard Operating Procedure “Blood Collection and Processing for Plasma and Whole Cell Components” in Appendix 4.
- F.4.b.(3). Plasma and buffy coat/red cell pack shall be stored at -70° to -80°C at the subcontractor’s facility until shipped to the CPTAC BCR.

F.4.c. Normal Tissue (when available)

- F.4.c.(1). Procuring normal tissue shall only be attempted when appropriate and must not compromise the generally accepted standard of patient care.
- F.4.c.(2). The procurement must conform to the Tissue Procurement Protocol contained in Appendix 2.
- F.4.c.(3). All tissue samples must be stored at vapor phase liquid nitrogen temperature at the subcontractor’s facility until shipped to the CPTAC BCR.

F.4.d. Shipping

- F.4.d.(1). Shipping will be arranged by the CPTAC BCR. The CPTAC BCR will provide the shipping container and pay for the costs of shipping.
- F.4.d.(2). Except for extraordinary circumstance preauthorized by the SAIC-F TPM, individual shipments will be arranged for the tissues obtained from six or more cases.
- F.4.d.(3). Each case shall include a completed Clinical Collection Form containing details regarding procurement such as times, tissue weights, etc., along with minimal patient information.

F.5. Baseline Patient Data and Diagnostic Histopathological Data

- F.5.a. The Baseline Case Report Form will contain baseline patient data and status at the start of the initial treatment regimen. The de-identified information will be submitted to the CPTAC BCR via an electronic interface to a clinical data repository as soon as possible after tissue procurement.

- F.5.b. The subcontractor shall be responsible for obtaining pathology reports for the cases submitted to the BCR. The reports shall be de-identified and electronic copies submitted to the BCR as soon as reasonably possible after the tissue has been shipped. The reports shall be in English.
- F.5.c. The subcontractor shall be responsible for obtaining high-quality electronic images of the FFPE slides on which the histology reports are based and submitting those to the BCR. The image format and other details will be provided by the BCR when it is operational. If electronic images are not readily available, the subcontractor shall send representative glass slides of the case to the BCR where images will be created. In this case, the slides will be returned to the subcontractor.

#### F.6. Long-Term Patient Follow Up

- F.6.a. The one year Case Report Form will contain patient data and status one year after start of the initial treatment regimen. The de-identified information will be submitted to the CPTAC BCR via an electronic interface to a clinical data repository.
- F.6.b. The five year Case Report Form will contain patient data and status five years after start of the initial treatment regimen. The de-identified information will be submitted to the CPTAC BCR via an electronic interface to a clinical data repository. **The five year follow up is not within the scope of this SOW and will be addressed at a later date.**
- F.6.c. Reasonable efforts will be expected to find patients for each follow up. Documentation describing the efforts to find any patients that have been lost to follow up will be submitted to the CPTAC BCR.

### G. Deliverables

The following table contains a list of deliverables that will be required.

#### G.1. Deliverable Summary and Due Dates

Deliverable	Due Date
IRB Approval	When executed
Material Transfer Agreement/Data Use Agreement	When executed
Participating Subject (Tumor Sample) Biospecimen and Submission Report Form	Recurring
Participant Subject Baseline Case Report Form/Diagnostic Histopathology	Recurring
Participant Subject One Year Case Report Form	Recurring

## G.2. Deliverable Descriptions and Acceptance Criteria

### G.2.a. IRB Approval

The subcontractor shall obtain local IRB approval for the work to be performed at their institution(s) and submit copies of the final approval and supporting documents to the CPTAC BCR and the SAIC-F TPM. The subcontractor shall also obtain a renewal of the approval for the second year of the Period of Performance. Electronic copies of the documents shall be submitted via email to the CPTAC BCR with a cc to the SAIC-F TPM.

#### **Acceptance Criteria**

Acceptable IRB approvals will be in a format consistent with local usage and allow the subcontractor to perform all the tasks in the SOW and their proposal. Scanned versions of the signed IRB approval document(s) in PDF format shall be acceptable.

### G.2.b. Material Transfer Agreement/Data Use Agreement

The subcontractor shall develop a MTA/DUA using the CPTAC template that includes the CPTAC BCR and obtain the needed local approval(s). Electronic copies of the documents shall be submitted via email to the CPTAC BCR and SAIC-F TPM. Scanned versions of the fully executed agreement(s) in PDF format shall be acceptable.

#### **Acceptance Criteria**

Acceptable MTAs/DUAs shall be in a format consistent with local usage, cover all the elements noted in the CPTAC template, and provide for the transfer of the materials and data use consistent with CPTAC policy.

### G.2.c. Participating Subject (Tumor Sample) Biospecimen and Submission Report Form

The subcontractor shall obtain the biospecimens (tissues and blood) from properly consented and enrolled participants and store the biospecimens locally per the appropriate tissue procurement protocol until shipping arrangements are made. For each participating subject, the subcontractor shall open a new case with the CPTAC BCR and complete the appropriate Case Submission Form via an electronic interface to the clinical data repository hosted by the CPTAC BCR. The CPTAC BCR shall ensure the completeness of the submitted form: any discrepancies noted by the CPTAC BCR shall be corrected by the TSS.

When notified by the BCR, the subcontractor shall package and ship the frozen biospecimens (tissues and blood) from each case per the instructions from the CPTAC BCR. The CPTAC BCR will provide appropriate shipping containers and pay for the costs of shipping. The frequency of shipments and the number of cases per shipment shall be determined by the CPTAC BCR.

**Acceptance Criteria**

All samples that have a fully completed Case Submission Form and approved for shipment from the CPTAC BCR shall be considered accepted when received by the CPTAC BCR.

*Note that the performance of each TSS will be monitored over time and if a pattern emerges where major discrepancies are noted between the samples submitted and the histopathologic analyses, the acceptance criteria for this deliverable may be adjusted.*

**G.2.d. Participant Subject Baseline Case Report Form/Diagnostic Histopathology**

Once the biospecimens associated with a case submitted to the CPTAC BCR have been qualified, the CPTAC BCR shall notify the TSS that a completed Baseline Case Report Form, diagnostic histopathology materials, and a de-identified copy of the original surgical pathology report should be submitted. The subcontractor shall complete the appropriate Case Baseline Form and submit it via an electronic interface to the clinical data repository hosted by the CPTAC BCR. The CPTAC BCR shall ensure the completeness of the submitted form; any discrepancies noted by the CPTAC BCR shall be corrected by the TSS.

The subcontractor shall also obtain and submit a de-identified copy of the surgical pathology report by email to the CPTAC BCR with a cc to the SAIC-F TPM. Finally, the subcontractor shall obtain the histopathology materials described in the relevant tissue procurement protocol (e.g., H&E slides). For the latter, electronic images may be produced and submitted to the CPTAC BCR; the TSS should consult with the CPTAC BCR regarding the details of electronic imaging (e.g., magnification, file format, etc.). If electronic images are not available, the TSS should contact the CPTAC BCR for instructions on how to ship the slides. Slides shipped to the CPTAC BCR will be imaged there and returned to the TSS.

**Acceptance Criteria**

Acceptable Baseline Case Report Forms will have all relevant fields completed with any discrepancies noted by the CPTAC BCR corrected.

Acceptable pathology reports must be complete, legible, and provided in English (cannot be extracted).

Acceptable histopathology slides or images must be of a quality suitable for evaluation by a pathologist and representative of the diagnosis. Images shall be submitted at the magnification and in the file format requested by the CPTAC BCR.

#### G.2.e. Participant Subject One Year Case Report Form

Approximately one year after the procurement of tissue from a participant, the Subcontractor shall attempt to follow up on the participant's clinical status. The subcontractor shall complete the appropriate One Year Case Report Form and submit it via an electronic interface to the clinical data repository hosted by the CPTAC BCR. The CPTAC BCR shall ensure the completeness of the submitted form; any discrepancies noted by the CPTAC BCR shall be corrected by the TSS.

##### **Acceptance Criteria**

Acceptable One Year Case Report Forms will have all relevant fields completed with any discrepancies noted by the CPTAC BCR corrected.

In the instance where a participant appears to have been lost to follow up despite a good-faith and reasonable effort on the part of the Subcontractor to find the patient or his or her record, documentation describing the efforts taken will be accepted in lieu of the a completed One Year Case Report Form.

#### G.3. General Acceptance Criteria

In addition to specific acceptance criteria listed above, general quality measures, as set forth below, will be applied to each deliverable received from the subcontractor under this Statement of Work.

- Accuracy – Deliverables shall be accurate in presentation, technical content, and adherence to accepted elements of style.
- Clarity – Deliverables shall be clear and concise. Any/all diagrams shall be easy to understand and be relevant to the supporting narrative.
- Consistency to Requirements – All deliverables must satisfy the requirements of this Statement of Work.
- Timeliness – Deliverables shall be submitted on or before the due date specified in the Subcontract, or submitted in accordance with a later scheduled date determined by the SAIC-F TPM.

All deliverables and correspondence must be in English.

#### **H. Meetings**

Participation in the following meetings is **required** during the Period of Performance.

## H.1. Kick Off

An initial kick off meeting will be held within 10 working days of award or as agreed to by the SAIC-F TPM. This will be attended by the SAIC-F TPM and SAIC-F CS, the NCI Project Officer, and representatives from the CPTAC Program Office. Key Subcontractor personnel as well as a representative from the Subcontractor's contracts organization are required to attend. The intent of the meeting is for all key personnel to meet to discuss the project's overall technical and contractual requirements.

At this meeting, the Subcontractor shall be prepared to discuss the following:

- Technical objectives.
- Deliverables and deliverable acceptance criteria.
- Reporting and invoice requirements.

## H.2. Monthly Project Team Meeting

A monthly teleconference will be held amongst the project team, the SAIC-F TPM, the NCI Project Officer, representatives from the CPTAC Program Office, and a representative from the CPTAC BCR. The SAIC-F TPM will oversee the meeting. The purpose of the meeting is to review the project's status, update the Subcontractor on the latest Program status, and ensure open and ongoing communication amongst all the stakeholders and participants in the Subcontractor-specific tissue procurement activities.

## H.3. Monthly CPTAC TSS Program Teleconference

A monthly teleconference will be held amongst all the CPTAC TSSs sponsored by the CPTAC Program Office to review overall Program status and ensure open communications amongst all the participants in the CPTAC tissue procurement activities.

## H.4. CPTAC Annual Meeting

The Subcontractor shall send at least one team member to the CPTAC Annual Meeting. Tentative location of the annual meeting is the Washington, D.C. metro area.

# **I. Reporting Requirements**

None. Monthly meetings will be used to measure project's progress.

**APPENDIX 1 – ACRONYMS**

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List of Acronyms

BCR – Biospecimen Core Resource  
CPTAC – Clinical Proteomics Tumor Analysis Consortium  
DCC – Data Coordinating Center  
DNA – Deoxyribonucleic Acid  
DUA – Data Use Agreement  
GSC – Genomic Sequencing Centers  
HIPAA – Health Insurance Portability and Accountability Act  
IRB – Institutional Review Board  
LDS – Limited data set  
MTA – Material Transfer Agreements  
NCI – National Cancer Institute  
PCC – Protein Characterization Center  
PHI – Protected Health Information  
PMP – Project Management Plan  
QC – Quality Control  
RNA – Ribonucleic Acid  
SAIC-F – SAIC Frederick, Inc.  
SOP – Standard Operating Procedures  
SOW – Statement of Work  
TCGA – The Cancer Genome Atlas  
TPM – Technical Project Manager  
TSS – Tissue Source Site

**APPENDIX 2**

**ACCEPTABLE TUMOR TYPES AND COLLECTION PROTOCOLS**



## **Prospective Biospecimen Collection Protocol**

### **Breast Cancer**

**v1.0**

#### **Overview**

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) sponsored by the NCI Office of Cancer Clinical Proteomics Research is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. The overarching goal of CPTAC is to improve our ability to diagnose, treat and prevent cancer. To achieve this goal in a scientifically rigorous manner, the NCI launched CPTAC to systematically identify proteins that derive from alterations in cancer genomes and related biological processes, and provide this data with accompanying assays and protocols to the public.

CPTAC consists of a network of Proteome Characterizations Centers (PCC) and a Data Coordinating Center (DCC) serving as a hub and central repository for all CPTAC data. CPTAC will be expanded to include a 1) network of Tissue Source Sites (TSS) to obtain clinical specimens for proteomic and genomic analysis, 2) a Biospecimen Core Resource (BCR) to serve as a repository for tissue and associated, de-identified clinical data submitted to the program, and 3) a Genomic Characterization Center (GCC) dedicated to the genomic analysis of CPTAC specimens.

#### **Purpose**

The purpose of this protocol is to establish the minimum procurement parameters for ductal and lobular breast cancer stage IIA – IIIC specimens to be submitted to the CPTAC for proteomic and genomic analysis. The tissue source will be from newly diagnosed, untreated patients undergoing definitive surgery for breast cancer.

The protocol builds on CPTAC experience with human tissues obtained from the TCGA programs and specifically aims for:

- Minimized specimen processing and ischemia time with the ischemia time recorded.
- Sufficient total material from each patient divided into multiple samples suitable for independent processing for proteomic and genomic analysis.
- Independent samples suitable for histopathological analysis with frozen sections obtained at the BCR.
- Improved determination of weights of individual samples for improved estimates of protein yield.

#### **Scope**

The protocol applies to any samples submitted by a SAIC-F subcontractor to the CPTAC BCR.

**CTPAC Prospective Biospecimen Collection Protocol - Breast Cancer**

**Version 1.0 (12/2012)**

**p. 1**

**Requirements*****Patient Inclusion Criteria***

- Newly diagnosed patients with invasive breast cancer undergoing definitive surgery for breast cancer.

***Patient Exclusion Criteria***

- Prior history of other malignancies within the past 12 months other than treated basal cell carcinoma of the skin or treated DCIS of the contra lateral breast (as long as no tamoxifen was administered).
- Other malignancies at the time of surgery.
- Prior systemic chemotherapy for any cancer.
- Radiation or chemotherapy for the invasive breast cancer.
- Prior history of radiation therapy involving the breast such as mantle field radiation for Hodgkins Disease, radiotherapy for lung cancer, etc.
- Patients who are found to have diagnosis other than invasive breast cancer.

***Regulatory (before procurement)***

- IRB approval received and documented with BCR.
- MTA/DUA agreement received and documented with BCR.

***Tissue Procurement and Shipping***

- Signed patient consent (maintained at the tissue source site, copy to CPTAC/BCR not required).
- Cancer tissue per protocol.
- Normal tissue per protocol.
- Blood per SOP.
- Shipping Manifest completed and submitted.
- Clinical Quality Control Form (contains details regarding procurement such as times, tissue weights, etc. along with minimal patient information) completed and submitted.
- Adherence to BCR shipping instructions (the BCR will provide the shipping cryoport and cover the cost of shipping).

***Patient Data (after shipping)***

- History and status at surgery (specific data to be collected to be determined).
- Pathology Report (de-identified) including ER, PgR, and HER2 status.
- FFPE H&E diagnostic slides/images (at least one that is representative of the diagnosis in the pathology report; slides will be returned).
- Ten 5 micron unstained FFPE slides from the definitive surgical specimen submitted.
- Updated history and status one year after completion of the initial treatment regimen (data on neoadjuvant response if relevant and adjuvant/neoadjuvant treatment administered and other specific data to be collected to be determined).
- Updated history and status five years after completion of the initial treatment regimen (data on relapse and vital status along with other specific data to be collected to be determined).

***Tumor Specimen Inclusion Criteria***

- Greater than 500 mg total of all tumor samples obtained from a patient (including the weight of the cores).
- Greater than 60% tumor cell nuclei (tumor cell enrichment procedures may be allowable).
- Less than 20% necrosis.

**Tissue Procurement Procedure (Two Step Procedure for Tumor Tissue)**

***Core Biopsies of Tumor before Devascularization of Tumor***

- Obtain core biopsies (minimum of 4) with a 14 gauge biopsy needle
- Place in pre-labeled cryovials and freeze in liquid nitrogen vapor.

***Larger Sample Accrual from Excised Tumor from Same Patient***

- Record time when the tumor is surgically devascularized.
- Process through pathology within 30 minutes of removal from patient (specimen grossing must therefore be done as soon as possible after the tumor is removed).
- Accrue as much material possible while maintaining the integrity of tissue needed for clinical diagnostics.
- Divide the tumor specimen into at least five ~100 mg pieces for submission to the BCR. Weigh each piece and record. The size of the samples should allow them to fit into the cryovials with little to no compression.
- Additional samples may be obtained for local use.
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor.
- Record time when samples are place in the liquid nitrogen vapor.

***Normal Breast Tissue from Same Patient***

- Identify normal appearing breast tissue as far from the tumor as possible and excise without interfering with surgical-margin analysis. Alternatively, if a surgical procedure is to be performed on the contralateral breast for cosmetic reasons, collect normal-appearing breast tissue from that procedure.
- Divide the tissue into ~200 mg samples.
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor.

**Blood Collection Procedure**

- Obtained pre-operatively.
- 10 ml lavender top vacutainer with the blood processed per SOP.



## Prospective Biospecimen Collection Protocol

### Colon Cancer

v1.0

#### Overview

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) sponsored by the NCI Office of Cancer Clinical Proteomics Research is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. The overarching goal of CPTAC is to improve our ability to diagnose, treat and prevent cancer. To achieve this goal in a scientifically rigorous manner, the NCI launched CPTAC to systematically identify proteins that derive from alterations in cancer genomes and related biological processes, and provide this data with accompanying assays and protocols to the public.

CPTAC consists of a network of Proteome Characterizations Centers (PCC) and a Data Coordinating Center (DCC) serving as a hub and central repository for all CPTAC data. CPTAC will be expanded to include a 1) network of Tissue Source Sites (TSS) to obtain clinical specimens for proteomic and genomic analysis, 2) a Biospecimen Core Resource (BCR) to serve as a repository for tissue and associated, de-identified clinical data submitted to the program, and 3) a Genomic Characterization Center (GCC) dedicated to the genomic analysis of CPTAC specimens.

#### Purpose

The purpose of this protocol is to establish the minimum procurement parameters for colon adenocarcinoma (biopsy proven) specimens to be submitted to the CPTAC for proteomic and genomic analysis. The tissue source will be from newly diagnosed, untreated patients undergoing definitive surgery for colon cancer.

The protocol builds on CPTAC experience with human tissues obtained from the TCGA programs and specifically aims for:

- Minimized specimen processing and ischemia time with the ischemia time recorded.
- Sufficient total material from each patient divided into multiple samples suitable for independent processing for proteomic and genomic analysis.
- Independent samples suitable for histopathological analysis with frozen sections obtained at the BCR.
- Improved determination of weights of individual samples for improved estimates of protein yield.

#### Scope

The protocol applies to any samples submitted by a SAIC-F subcontractor to the CPTAC BCR.

## **Requirements**

### ***Patient Inclusion Criteria***

- Newly diagnosed, untreated patients undergoing primary surgery for colon adenocarcinoma.

### ***Patient Exclusion Criteria***

- Prior history of other malignancies within the past 12 months except basal cell carcinoma of the skin.
- Other malignancies at the time of surgery.
- Prior systemic chemotherapy for any cancer.
- Radiation or chemotherapy for the colon cancer.
- Prior radiation therapy to the abdomen or pelvis for any cancer.

### ***Regulatory (before procurement)***

- IRB approval received and documented with BCR
- MTA/DUA agreement received and documented with BCR

### ***Tissue Procurement and Shipping***

- Signed patient consent (maintained at the tissue source site, copy to CPTAC/BCR not required).
- Cancer tissue per protocol.
- Normal tissue per protocol.
- Blood per SOPs.
- Shipping Manifest completed and submitted.
- Clinical Quality Control Form (contains details regarding procurement such as times, tissue weights, etc. along with minimal patient information) completed and submitted.
- Adherence to BCR shipping instructions (the BCR will provide the shipping cryoport and cover the cost of shipping).

### ***Patient Data (after shipping)***

- History and status at surgery (specific data to be collected to be determined).
- Pathology Report (de-identified).
- FFPE H&E diagnostic slides/images (at least one that is representative of the diagnosis in the pathology report; slides will be returned).
- Updated history and status one year after completion of the initial treatment regimen (specific data to be collected to be determined).
- Updated history and status five years after completion of the initial treatment regimen (specific data to be collected to be determined).

### ***Tumor Specimen Inclusion Criteria***

- Greater than 200 mg total of all tumor samples obtained from a patient.
- Greater than 60% tumor cell nuclei.
- Less than 20% necrosis.

**Tissue Procurement Procedure**

- Record the time point for initial ligation of the arterial blood supply to the tumor.
- Remove the particular section of the colon of interest with the goal of minimizing time of ischemia to the tissue. Record the time of removal.
- Excise a ~1 g portion of the tumor mass and a separate ~2 g portion of adjacent normal colonic tissue. Place both specimens placed into separate specimen containers. The weight of each gross sample will be obtained and recorded.
- Divide the tumor and normal specimens into ~100 mg pieces for submission to the BCR. Weigh each piece and record. The size of the samples should allow them to fit into the cryovials with little to no compression. At least three samples must be submitted to the BCR.
- Additional samples may be obtained for local use.
- Place each piece of tissue destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor.
- Record time when samples are place in the liquid nitrogen vapor.

**Blood Collection Procedure**

- Obtained preoperatively.
- 10 ml lavender top vacutainer with the blood processed per SOP.



## Prospective Biospecimen Collection Protocol Ovarian Cancer v1.0

### Overview

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) sponsored by the NCI Office of Cancer Clinical Proteomics Research is a comprehensive and coordinated effort to accelerate the understanding of the molecular basis of cancer through the application of robust, quantitative, proteomic technologies and workflows. The overarching goal of CPTAC is to improve our ability to diagnose, treat and prevent cancer. To achieve this goal in a scientifically rigorous manner, the NCI launched CPTAC to systematically identify proteins that derive from alterations in cancer genomes and related biological processes, and provide this data with accompanying assays and protocols to the public.

CPTAC consists of a network of Proteome Characterizations Centers (PCC) and a Data Coordinating Center (DCC) serving as a hub and central repository for all CPTAC data. CPTAC will be expanded to include a 1) network of Tissue Source Sites (TSS) to obtain clinical specimens for proteomic and genomic analysis, 2) a Biospecimen Core Resource (BCR) to serve as a repository for tissue and associated, de-identified clinical data submitted to the program, and 3) a Genomic Characterization Center (GCC) dedicated to the genomic analysis of CPTAC specimens.

### Purpose

The purpose of this protocol is to establish the minimum procurement parameters for high-grade serous ovarian, fallopian tube, and peritoneal cancer specimens to be submitted to the CPTAC for proteomic and genomic analysis. The tissue source will be from newly diagnosed, untreated patients undergoing definitive surgery for ovarian cancer.

The protocol builds on CPTAC experience with human tissues obtained from the TCGA programs and specifically aims for:

- Minimized specimen processing and ischemia time with the ischemia time recorded.
- Sufficient total material from each patient divided into multiple samples suitable for independent processing for proteomic and genomic analysis.
- Independent samples suitable for histopathological analysis with frozen sections obtained at the BCR.
- Improved determination of weights of individual samples for improved estimates of protein yield.

### Scope

The protocol applies to any samples submitted by a SAIC-F subcontractor to the CPTAC BCR.

**Requirements*****Patient Inclusion Criteria***

- Newly diagnosed, untreated patients undergoing primary cytoreductive surgery for serous ovarian cancer.
- Tumor from ovary, pelvic mass or omentum only (other anatomic sites not acceptable).

***Patient Exclusion Criteria***

- Prior history of other malignancies within the past 12 months except non-melanomatous skin cancer and in situ cervical cancer.
- Other malignancies at the time of surgery.
- Prior systemic treatment (cytotoxic or molecular) for any malignancy.
- Prior radiation therapy for any prior malignancy that involves treatment to the abdomen or pelvis.
- Prior hormonal therapy within the last five years for cancer.
- Patients who are found to have low-grade (grade 1) or low stage (stage I or II) serous ovarian, fallopian tube, or peritoneal cancer based on final pathology (typically 5-10 days after surgery).

***Regulatory (before procurement)***

- IRB approval received and documented with BCR.
- MTA/DUA agreement received and documented with BCR.

***Tissue Procurement and Shipping***

- Signed patient consent (maintained at the tissue source site, copy to CPTAC/BCR not required).
- Cancer tissue per protocol.
- Normal fallopian tube fimbriae if possible (per Crum protocol)
- Blood per SOPs.
- Shipping Manifest completed and submitted.
- Clinical Quality Control Form (contains details regarding procurement such as times, tissue weights, etc. along with minimal patient information) completed and submitted.
- Adherence to BCR shipping instructions (the BCR will provide the shipping cryoport and cover the cost of shipping).

***Patient Data (after shipping)***

- History and status at surgery (specific data to be collected to be determined).
- Pathology Report (de-identified)
- FFPE H&E diagnostic slides/images (at least one that is representative of the diagnosis in the pathology report; slides will be returned).
- Updated history and status one year after completion of the initial treatment regimen (specific data to be collected to be determined).
- Updated history and status five years after completion of the initial treatment regimen (specific data to be collected to be determined).

***Tumor Specimen Inclusion Criteria***

- Greater than 300 mg total of all samples obtained from a patient.
- Greater than 60% tumor cell nuclei.
- Less than 20% necrosis.
- Less than 10 minutes warm ischemia time.

**Tissue Procurement Procedure**

***Tumor Tissue***

- Identify a 1-2 cc nodule that appears to be mostly tumor, with little or no intervening normal tissue.
- Dissect free from surrounding attachments leaving main blood supply intact for as long as possible unless specimen is to be excised immediately from within a larger tumor mass.
- Start timer when blood supply transected.
- Take nodule off operating field onto back table, bisect to confirm apparent tumor.
- Cut at least three strips of tumor each measuring 8-10 mm x 2-3 mm x 2-3 mm (~100 mg each) for submission to the BCR.
- Weigh each strip and record.
- Additional samples may be obtained for local use.
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor.
- Record time when samples are placed in the liquid nitrogen vapor.

***Normal Tissue (Fallopian tube submitted for SEE-FIM sectioning)***

- Record the time of excision.
- If a fallopian tube grossly appears normal after SEE-FIM, collect 2-3 individual fimbria from that tube.
- Weigh each piece and record.
- Place each piece destined for the BCR into a pre-labeled cryovial and freeze in liquid nitrogen vapor.
- Record time when samples are placed in the liquid nitrogen vapor.

**Blood Collection Procedure**

- Obtained preoperatively.
- 10 ml lavender top vacutainer with blood processed per SOP.

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**APPENDIX 3 – IRB GUIDANCE DOCUMENT**

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The purpose of this document is to assist Institutional Review Boards (IRBs)/Ethics Boards and/or Privacy Boards at participating clinical sites in their review of protocols that include submission of tissues and associated clinical data to The Clinical Proteomics Tumor Analysis Consortium (CPTAC) Project of the National Cancer Institute (NCI) of the National Institutes of Health (NIH). This document provides summary information on the project and how it works, followed by a discussion of key points of interest to this audience.

**A. CPTAC Aim and Summary**

The overarching goal of CPTAC is to improve our ability to diagnose, treat, and prevent cancer. To achieve this goal in a scientifically rigorous manner, the National Cancer Institute (NCI) launched CPTAC to systematically identify proteins that derive from alterations in cancer genomes and related biological processes, and provide this data with accompanying assays and protocols to the public.

Genomics initiatives such as The Cancer Genome Atlas (TCGA) have characterized and sequenced the genomic alterations from several types of cancer. These efforts are providing a catalogue of alterations in the cancer genomes and setting the stage for the development of more molecular interventions. CPTAC will leverage its analytical outputs from Phase I in the coming years by producing a unique continuum that defines the proteins translated from cancer genomes in order to link genotype to proteotype and ultimately to phenotype. This goal will be met through four overarching objectives. They are:

Objective 1: Identify and characterize the protein inventory from tumor and normal tissue biospecimens

Objective 2: Integrate genomic and proteomic data from analysis of common cancer biospecimens

Objective 3: Develop assays against proteins prioritized in the discovery stage as potential biomarker candidates

Objective 4: Perform testing of verification assays in relevant cohorts of biospecimens

For the cancer types studied, approximately 100 cases of tumor tissue with a case-matched germline DNA source that have been or will be genomically analyzed across multiple genomic platforms will be characterized by large-scale, quantitative protein profiling via mass spectrometry. When possible, matched normal tissue for each case will be included in the analyses. Each case will be obtained with demographic and clinical annotation, along with follow-up information minimally sufficient to correlate molecular profiles with survival.

CPTAC is operating as a network of grant and contract funded entities. With regard to prospective human sample collection, clinically annotated tissue specimens will be collected from several

participating CPTAC Tissue Source Sites (TSS), and sent to the CPTAC Biospecimen Core Resource (BCR). The BCR will perform quality control on the tissues and will send qualified samples to the CPTAC Protein Characterization Centers (PCC) for proteomic analysis. The BCR will use uniform protocols to isolate nucleic acids that will be sent to a Genomic Sequencing Center (GSC) within the network for genomic analysis. The PCC and GSC data are sent to the CPTAC Data Coordination Center (DCC), where the data are made available to other investigators via the internet. Raw sequencing data may be maintained by a separate DCC than the rest of the CPTAC data. The BCR will also standardize and quality control the participant clinical data that are subsequently sent directly to the central DCC.

The GSC molecular characterizations will include whole-exome sequencing, micro- and messenger-RNA expression profiling (sequenced based), and chromosomal structure and copy number alteration (low pass sequence and/or chip based). Since both tumor and germline DNA are sequenced from each case, somatic single nucleotide variants are discovered. However, the germline information is also available for which investigators can use for their research. Proteomic characterization of these samples by the PCCs will include mass spectrometry-based profiling of the proteome, phosphoproteome, and glycoproteome of these specimens. A subset of selected samples may also be characterized by protein microarray and/or reverse-phase protein

## **B. Key Human Subjects Policies**

This document was written to provide guidance to Principal Investigators and IRB staffs at the CPTAC TSSs at which the participants are enrolled and their tissue specimens and clinical data are collected. CPTAC will collect tissues and associated clinical data from US-based organizations using SAIC-F subcontracting mechanisms.

U.S.-based sites are subject to federal regulations covering human subjects research (45 CFR 46, the “Common Rule”) and are also HIPAA “Covered Entities.” The following sections describe key CPTAC protocols and policies relevant to human subject research and participant protection policies.

## **C. Minimal Risk Protocol**

To date, most IRBs have considered protocols providing clinically annotated tumor tissues to programs such as The Cancer Genome Atlas (TCGA) program sponsored by the National Cancer Institute (NCI) and National Human Genome Research Institutes (NHGRI) to be “minimal risk.” The CTPAC program will mimic TCGA program in all aspects relating to patient risk. The CPTAC program will employ a series of prospective protocols for tissue acquisition that are non-interventional and will employ a “surgical remnant” or “surgical discard” approach; i.e., the tissues to be collected will be obtained during the normal course of care for cancer patients that would normally be discarded or used in other research programs. Participants are at some “social risk” from potential loss of privacy or the possibility of a security breach resulting in a loss of confidentiality of their medical information. Participation in CPTAC holds an additional social risk: the project generates individually unique proteomic and genetic information (see Section G [Genetic Data: Open vs. Controlled-Access Tiers] below) and there is a

theoretical risk that such data combined with third-party databases could result in re-identification of a participant.

With “minimal risk” protocols, IRBs may wish to consider applications or amendments to existing protocols under an expedited review process.

#### **D. Linked Protocol and “Coded” Identifiers**

Similar to TCGA, CPTAC will operate as a “linked” protocol, with each participant ID being doubly de-referenced (i.e., “coded” twice) before tissue or data are distributed by the Network. The first linking key is retained by the TSS at which the participants are enrolled. Access to this key is the purview of TSS institutional policies and the local IRB. The second linking key is retained by the CPTAC BCR and is only made available within the program for quality control purposes upon approval by the Director, Office of Cancer Clinical Proteomics Research. The second key will also be provided to the TSS Principal Investigator upon presentation of IRB approval to have this second key. As a result of these policies, investigators using CPTAC data are prevented from seeing participant direct identifiers or from linking backwards to the primary participant identifiers at the TSS clinical sites by both technical systems and contractual obligations.

*“45 CFR 46.101(b)(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects”*

#### **E. HIPAA and Collection of a Limited Data Set (LDS)**

Clinical data will be provided by the CPTAC TSS to the CPTAC BCR in a form compliant with a HIPAA-defined Limited Data Set (LDS) (The 16 traditional direct identifiers as defined by HIPAA under 45 CFR 164.514(e)(2), name, social security number, etc. are excluded). Additionally, CPTAC will not collect geographic information at the level of detail permitted by an LDS. CPTAC will collect specific demographic and clinical event date information, for example, country of origin, dates of birth, death, admission, diagnosis, surgery, treatment, and release. These data are necessary for quality control purposes and to enable correlation of molecular profiles with time-based patient characteristics such as survival. It is expected that the organization hosting the BCR will be a subcontractor to SAIC-F and the BCR and SAIC-F will enter into HIPAA-compliant Data Use Agreements (DUA) with the clinical Tissue Source Sites (the HIPAA “Covered Entity”) to enable this process.

However, LDS data will **not** be distributed beyond the CPTAC DCC to any other CPTAC network component, (PCC and GSC) nor to the broader research community. Prior to data distribution, the DCC will convert all dates to intervals and/or modify dates to being no more specific than one year. As a result, distributed participant data meet the HIPAA test of being De-Identified (45 CFR 164.514(b)(2)(i)).

## **F. Informed Consent**

CPTAC policy is that subjects enrolled for tissue collections must be consented under a protocol that does not expressly conflict with any key concepts related to participation in CPTAC.

## **G. Genetic Data: Open vs. Controlled-Access Tiers**

In addition to proteomic data, CPTAC will generate individually unique genetic data (“genetic fingerprints”, or genotypes). These data will not be directly tied to an identified individual, and the clinical information associated with these data are de-identified as described above. Nevertheless, a theoretical risk exists that the genetic data in conjunction with third party databases (e.g., forensic genetic profile databases) could lead to the re-identification of a participant or relative. Consequently, NIH policy for CPTAC will be the same as for TCGA in that individual genetic data from the characterization studies will be kept in a restricted-access database. (More information on segmentation of all CPTAC data between the open-access and restricted-access tiers is in Section I2 below.)

To be authorized to access the restricted tier of data, Investigators will be required to submit an application to the project’s Data Access Committee (DAC). Upon approval by the DAC that the access request is for bona fide research purposes, the Investigator and their institution will be required to subscribe to a Data Use Certification that controls their ability to access the data, and places requirements for data security upon them, scientists directly under their control, and their institutions. Data use for these controlled-access data are for any legitimate research use (i.e. there are no data use restrictions and users may apply data to non-cancer research-related discovery).

## **H. IRB documentation of approval to participate**

NIH policy regarding TSS participation in CPTAC places 45CFR46 compliance responsibility on the local IRB. Nevertheless, to participate, each TSS Principal Investigator must have some level of IRB review and document such review to SAIC-Frederick (SAIC-F), the NCI, and the BCR. Such review can range from a full IRB protocol submission and approval, amendment to an existing protocol, or an expedited/administrative review. The IRB may determine that participation is either Exempt or grant a Waiver, either of which is acceptable to NIH. Also, the IRB may determine that participation is not human subjects research, if, for example, the subjects are deceased.

Regardless of the IRB finding, however, program policy is that a TSS Principal Investigator must document to SAIC-F, NCI and the BCR that their IRBs have either:

1. approved their participation specifically in the CPTAC project, through an approved protocol, amendment, exemption, or waiver, and the documentation must include **specific mention of CPTAC**; or
2. provided documentation that the IRB does not consider participation to constitute “human subjects research,” and therefore does not have purview.

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## I. Additional information on CPTAC Policies

### I.1. Human Subjects and Participant Protection

CPTAC expects investigators, their institutions, and their IRBs to consider, based on their own standards of research practice, whether or not research involving coded and potentially re-identifiable information in CPTAC datasets meets the definition of “human subjects research” or not. The NCI presumes that this determination will be made consistent with institutional policies and under the auspices of the local IRB.

#### I.1.a. Contents of Informed Consent, additional information

For the purpose of reviewing the content of Informed Consents for prospective collections, the following key concepts pertinent to CPTAC should be considered for inclusion and disclosure to participants:

- genetic research, including proteomic analysis and DNA sequencing
- sharing of biospecimens, including to collaborators at other institutions
- sharing of clinical data, including to collaborators at other institutions
- possibility of future research use
- use of internet-connected electronic database with restricted public access
- the risk of loss of privacy or confidentiality of their personal information
- there will be no return of individual results to the participant
- should a patient withdraw, the project cannot retrieve or delete data once they have been distributed. Residual tissue at the BCR will no longer be used.

CPTAC may develop Informed Consent templates with suggested language that includes the concepts above, with specific nuances for prospective tissue procurement protocols.

### I.2. Data Sharing and Access

#### I.2.a. Rapid and Broad Data Release

CPTAC policy is to promote wide dissemination of all project data for use by the biomedical research community and to assure their maximum utility. Accordingly, CPTAC is committed to the rapid and complete release of its datasets for use by all investigators throughout the global scientific community who, along with their institutions, certify their agreement with CPTAC policies.

### I.2.b. Data Access: open- versus restricted-access tiers

To minimize the risk of participant identification, the CPTAC Project Team established a policy that CPTAC data be made available from a two-tiered data access system.

- The Open-Access Data Tier will be publicly accessible to anyone on the internet and contain only proteomic, genomic, and clinical data that cannot be analyzed to generate a dataset unique to an individual. These data may include:
  - Tissue pathology data
  - HIPAA de-identified clinical data
  - Gene expression data
  - Copy-number alterations for non-genetic platforms
  - Proteomic data
  - Data summaries, such as genotype frequencies
  - DNA sequence data of single amplicons
- The Controlled-Access Data Tier will contain genomic and clinical data that are associated to a unique, but not directly identified, person. However, there is a risk that these data could be analyzed to potentially identify a person through reference to 3<sup>rd</sup> party databases. They will therefore be managed with both additional technical security and a qualification and access authorization process for investigators and their institutions. They will be made available to any qualified researcher for the purpose of biomedical research, once the investigator, along with his/her institution, has certified agreement to the statements within TCGA Data Use Certification (DUC). The DUC can be found at:  
[http://dbgap.ncbi.nlm.nih.gov/aa/wga.cgi?page=DUC&view\\_pdf&stacc=phs000178.v4.p4](http://dbgap.ncbi.nlm.nih.gov/aa/wga.cgi?page=DUC&view_pdf&stacc=phs000178.v4.p4)

## **J. Description of CPTAC Components and Operations**

This appendix provides a more detailed description of the CPTAC network, specifically the various institutions that operate the “pipeline” that ultimately results in the CPTAC data sets being made available as a community resource.

J.1. In addition to the Tissue Source Sites (TSS), the TCGA Network is comprised of the following entities, working under a combination of grants and contracts from NCI and SAIC-F.

J.2. Biospecimen Core Resource (BCR)

A CPTAC BCR will be established as a central site for the receipt, review and processing of tissues and associated clinical data. The BCR will be the primary interface between the TSSs and the CPTAC Network.

Tissue samples, after screening against inclusion and exclusion criteria at the TSS, will be shipped to the BCR. Samples of tumor and, if available, normal tissue will be shipped from the BCR to the PCCs for proteomic analysis. In addition, nucleic acids will be isolated at the BCR. Subsequent proteomic and genomics analyses will be performed on tissues or analytes from samples that meet pathology quality control (QC) using uniform protocols. All protein, DNA, and RNA will be co-isolated from samples from the same individual such that characterizations are effectively performed on the same sample. These analytes are also subject to several QC processes. Subsequently, DNA and RNA will be distributed to the CPTAC GCC.

Clinical data associated with the samples will be collected from the TSS via electronic case report forms. At the BCR, the data will be quality controlled and transformed into a standardized caBIG-based terminology and a uniform data model, and then sent to the CPTAC DCC. Note that samples and associated data sent by the BCR to the PCCs and GSC for characterization are De-Identified.

The BCR will also ensure and verify that CPTAC human subjects protections policies, procedures, and regulations are followed.

The Biospecimen Core Resources for CPTAC will be established under subcontract by SAIC-F under the Federally-Funded Research and Development Center arrangement with the NCI.

J.3. Genomic Sequencing Center (GSC)

The Genomic Sequencing Centers (GSC) will conduct DNA- and RNA-based molecular characterizations.

The GSC will perform large-scale DNA sequencing using the latest sequencing technologies. All CPTAC samples will be analyzed by whole exome sequencing to reveal mutations within coding regions.

The GSC will receive samples from the CPTAC BCR and log them into local material management / laboratory information system (LIMS) databases. The GSC will also have access to sample logistics and QC data from the BCR, as necessary, and may store local copies of such data for operational support. Center databases will maintain the link between the CPTAC IDs provided

by the BCR and the derived data. The molecular characterization data generated by the GSC will be sent to the CPTAC Data Coordinating Center (DCC), where they will be integrated with the clinical and tissue specimen data sent by the BCR.

The Genomic Sequencing Center for CPTAC will be established under subcontract by SAIC-F under the Federally-Funded Research and Development Center arrangement with the NCI.

#### J.4. Proteome Characterization Centers (PCCs)

The CPTAC consists of five teams that create a network of PCCs. The PCCs are:

- Boise State University, Boise, ID
- Broad Institute, Cambridge, MA
- Fred Hutchinson Cancer Research Center, Seattle, WA
- Harvard Affiliated Hospitals, Boston, MA
- Johns Hopkins University, Baltimore, MD
- Massachusetts Institute of Technology, Cambridge, MA
- Massachusetts General Hospital. Boston, MA
- Memorial Sloan-Kettering Cancer Center, New York, NY
- New York University, New York, NY
- Oregon Health & Science University, Portland, OR
- Pacific Northwest National Laboratory, Richland, WA
- Stanford University, Stanford CA
- University of California at San Diego, San Diego, CA
- University of Chicago, Chicago, IL
- University of Connecticut Health Center, Farmington, CT
- University of North Carolina, Chapel Hill, NC
- University of Texas M.D. Anderson Cancer Center, Houston, TX
- University of Washington, Seattle, WA
- Vanderbilt University, Nashville, TN

- Virginia Polytechnic Institute and State University, Northern Virginia Center, Fall Church, VA
- Washington University in St. Louis, St. Louis, MO

#### J.5. Data Coordination Center (DCC)

The Data Coordination Center (DCC) is the main data repository of CPTAC, and coordinates technical data standards across the entire project. The DCC collects, stores and distributes the proteomic, clinical, and genomic data generated by the project. The DCC links together all data generated by the project into a single integrated resource, including clinical information that will be extracted from medical records by TSSs (via the BCR) and the raw results from the PCCs and GSC

To help ensure the protection of participants consistent with the policies of CPTAC, the DCC software includes security systems to control access, and data verification and modification tools to prevent content from being readily used to identify participants. In no case will the DCC database include any direct identifiers such as name, medical record number, address, social security numbers, or contact information. The Limited Data Set received from any TSS is immediately modified to meet the HIPAA definition of De-Identified by exclusion of all the 18 identifiers cited in the Privacy Rule.

While CPTAC employs one main DCC, data may actually be housed at multiple databases at the National Institutes of Health, with the data divided up according to the technical requirements for storage. For example, some CPTAC sequence data may also be deposited in the NIH Database of Genotypes and Phenotypes (dbGAP). The overall data access restriction policies developed by CPTAC apply to CPTAC data regardless of where they are technically stored.

The main CPTAC Data Coordinating Center is housed at the Georgetown University under a direct government contract to ESAC, Inc., Rockville, MD.



**APPENDIX 4 - STANDARD OPERATING PROCEDURES**

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## Blood Collection and Processing for Plasma and Whole Cell Components

v1.0

### PURPOSE

The purpose of this protocol is to establish a uniform procedure for collecting and processing blood samples obtained as part of the CPTAC prospective tissue procurement project. The blood samples are intended to provide 1) plasma for subsequent biomarker discovery and 2) cellular blood components for germ line genetic analysis of tissue donors.

### BACKGROUND

This procedure was originally developed to provide plasma samples for CPTAC-wide experimentation collected under similar blood collection and plasma processing conditions, to assure, as much as possible, that differences in molecular profiles of such specimens will not be due primarily to different collection and processing conditions. The common procedure for obtaining plasma was developed after analysis of many protocols in use and an examination of the available scientific rationales for different steps in these protocols, as well as the reasonable accommodations to a common protocol required by the different program sites. Note in particular that the use of refrigeration in processing, as prescribed here, can result in platelet activation and thus may result in molecular profiles that are distinct from protocols performed at room temperature. The original procedure has been expanded to include the collection and storage of the cellular blood components remaining after fractionation to be used for determining the germ line genetics of patients providing tumor and normal tissue to the CPTAC.

This procedure assumes that informed consent has been obtained and a method for tracking consent is in place.

The original procedure was adapted from the NCI/EDRN/SPORE Lung Cancer Biomarkers Group SOP for Collection of Serum and Plasma Samples for Proteomic Analysis HUPPO's recommended SOP for EDTA-Plasma Specimen Collection (Plasma Proteome Project, 2006).

### SCOPE

The protocol applies to any samples submitted by a SAIC-Frederick subcontractor to the CPTAC Biospecimen Core Resource (BCR).

### MATERIALS

1. Rubber (non-latex) band for tourniquet
2. Antiseptic wipes
3. 21-23 gauge Butterfly needle with attached tubing and Luer adapter
4. Extra Vacutainer® (small, any type) for collecting the initial stream of blood (unless the EDTA tube is drawn later in a blood draw of multiple tubes)
5. Ice bucket and ice for chilling tubes
6. Refrigerated centrifuge capable of spinning samples at 1500-2000 g

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7. 10 mL lavender-top K2 EDTA BD Vacutainer® venous blood collection tubes (BD 366643, 10 mL plastic, whole blood EDTA tube with lavender top)
8. Sterile disposable 10 mL pipettes
9. 15 mL polypropylene Falcon tube (BD 352196)
10. Simport 3 mL cryovial (Sim-T310-3A) and 10 mL cryovial (Sim-T310-10A); pre-labeled per instructions from the CPTAC BCR

**PROCEDURES**

I. BLOOD COLLECTION

A. Patient position

1. Patient must be seated at least 5 minutes before the draw.
2. The arm should be positioned on a slanting armrest in a straight line from the shoulder to the wrist. The arm should not be bent at the elbow.

B. Source of blood

1. Median, cubital, basilic, or cephalic vein (never from a port).

C. Tourniquet technique

1. Apply a tourniquet 2 inches above the antecubital fossa or above area to be drawn with enough pressure to provide adequate vein visibility. Have the patient form a fist. Select the site for venipuncture.
2. Clean the forearm of the patient with antiseptic wipe in a circular motion beginning at the insertion site. Allow the antiseptic to dry.
3. Anchor the vein by placing the thumb 2 inches below the site and pulling the skin taut to prevent the vein from moving. The holding finger is placed below the site, not above, to prevent accidentally sticking the finger with the needle.
4. Using the dominant hand, insert either the Vacutainer® needle or the butterfly needle (if using Vacutainer® needle, attach hub first). Push the evacuated tube onto the Vacutainer® hub or the Luer adapter if using a butterfly.
5. Release the tourniquet once blood flow is established. [The elapsed time for the tourniquet should be less than 1 minute. In the case additional time is required, the tourniquet must be removed in a fashion that restores both the circulation and normal skin color.]
6. Make sure that tube additives do not touch the stopper or the end of the needle during venipuncture.

D. Drawing blood into K2 EDTA tubes

1. Pre-chill 10 mL lavender-top K2 EDTA BD Vacutainer® venous blood collection tubes (BD 366643, 10 mL plastic, whole blood EDTA tube with lavender top) on ice for at least 5 minutes.
2. Perform phlebotomy as described in Section C above.

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3. Collect approximately 3 mL of blood in an extra Vacutainer® and discard. [If the EDTA tube for CPTAC is in a later order of draw of multiple tubes, there is no need to collect this discard.]
4. Collect the CPTAC sample in the pre-chilled K2 EDTA Vacutainer®, completely fill the tubes. Carefully remove the tubes when full without dislodging the needle.
- E. Inversion of EDTA tubes
  1. Immediately after allowing the lavender-top Vacutainer® tube to completely fill, slowly and gently invert the tube 8-10 times.
  2. Immediately insert the tube into wet ice.
- II. PLASMA PROCESSING (Sample processing and freezing must be completed within 90 min of collection)
  - A. Centrifugation I
    1. Within 30 minutes of collection, centrifuge at 1500 g for 15 min in a refrigerated centrifuge (4° C).
  - B. Collection of supernatant I
    1. Transfer plasma (using sterile disposable 10 mL pipette) to centrifugation tubes (BD 352196, 15 mL polypropylene Falcon tube), taking care to not disturb the buffy coat.
    2. Recap Vacutainer® tube containing buffy coat and red cell mass and return to wet ice.
  - C. Centrifugation II
    1. The secondary tubes are then centrifuged at 2000 g at 4° C for 15 minutes to remove all potentially remaining cells.
  - D. Collection of supernatant II
    1. After second centrifugation, transfer the top 2.5 ml of the supernatant into a 3 ml cryovial (Simport Cryovial Sim-T310-3A).
    2. Additional aliquoting and storage to be determined by each site at their discretion.
  - E. Collection of buffy coat and red cell mass
    1. Transfer buffy coat and red cell mass (using sterile disposable 10 mL pipette) into a 10 mL cryovial (Sim Port Cryovial Sim T310-10A).
- III. STORAGE AND SHIPMENT
  - A. Storage at the collection and processing site
    1. Biospecimens should be immediately placed on dry ice or in a -70° to -80° C freezer.
    2. Biospecimens should be stored at -70° to -80° C before shipment to the CPTAC BCR.
    3. Biospecimens should be shipped to the CPTAC BCR per instructions from the BCR. The shipping schedule to be determined and tailored to the site.
  - B. Transfer and Shipment to CPTAC Biospecimen Core Resource
    1. Do not permit specimens to thaw while handling.
    2. Ship to the CPTAC BCR per instructions from the BCR.
    3. Ensure all required documentation is included with the shipment.

## **Attachment 2: Technical Proposal Information Requirements**

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## Technical Proposal Information Requirements

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Below is a synopsis of the technical information requested from Offerors. Refer to the RFP Document for other requirements and information. Offerors are asked to be direct and concise in presenting information that clearly describes the proposed project. Offerors should realize that the clarity of their proposals is important in communicating the overall project goals to reviewers and that a concise and well formulated proposal will be more easily reviewed and evaluated.

### General Considerations:

Technical proposals shall provide a discussion of the proposed work to enable a thorough review of the approach. Attention should be given to addressing each the specific Goals of the Statement of Work listed elsewhere in this document. In addition, Offerors are reminded that the subcontract shall be based on Fixed Unit Prices for a series of specific deliverables that map to the specific Goals noted above. Offerors are strongly encouraged to develop their proposals in a manner allowing the reviewers to identify the mapping of the deliverables to the specific Goals of the SOW. Offerors are also reminded that the proposed approach must adhere to the CPTAC Tissue Procurement Protocols and the blood processing SOP attached to this document. Offerors should routinely check the CPTAC web site (<http://proteomics.cancer.gov/programs/cptacnetwork>) for any updates to these documents.

### Specific Considerations:

In addition to the general considerations above, the Offeror shall address the following areas in their proposals:

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## Technical Proposal Information Requirements

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### A. Executive Summary ( 1 page limit)

The summary shall contain the most important elements from the sections below but shall at a minimum clearly specify the following elements:

- The specific tumor type to be obtained.
- The number and frequency of expected patients to be enrolled for submission of samples.
- A brief description of the qualifications of your organization/team including any Subcontractors and their roles.
- A brief description of the capabilities at your institution to process and store the tissue and blood samples.

The summary shall be on a separate page or include a section break before the rest of the proposal.

**B. Technical Approach (10 page limit)****B.1.a.(1). Understanding**

Provide your understanding of what needs to be done, the scope of the work, the estimated length of time for the project to accrue 125 qualified cases. Describe any expected challenges and how you are going to address those challenges.

**B.1.a.(2). Approach**

Describe your approach to the proposed work for and challenges to accomplishing the Goals of the SOW. Describe how this approach will meet both project and overall CPTAC objectives.

**B.1.a.(3). Capabilities**

Describe the physical resources (e.g., laboratory spaces, equipment such as centrifuges, etc.) that are available for the work. Specifically describe the ultra-cold storage (e.g., liquid nitrogen freezers) that will be used for the work and the means by which specimens will be tracked while stored at your organization.

**C. Team and Key Personnel (5 page limit)*****C.1. Introduction***

Introduce your organization and/or team here. Give an overview of the capabilities brought to address this effort.

***C.2. Organization and/or Team***

Describe each proposed individual's role and the percentage of their time that is being bid, and a brief description of their qualifications. Fuller experience descriptions should be included in the appendix.

***C.3. Personnel***

One individual shall be designated as a Key Personnel. This individual will play the role of Principal Investigator/Project Manager and be responsible for the scientific execution of the project.

Resume summaries should be included in this section and full resumes in the appendix. Include a description of your plan to address the loss of the Principal Investigator from the project if that were to occur.

**D. Experience and Past Performance (5 page limit)**

Describe the teams overall experience with development, processes, and technologies similar to those described in this solicitation. Clearly indicate which organization on your team is providing this experience.

Provide a description of projects of similar scope that have been successfully performed in the past that indicate the ability to perform on this effort.

**E. Management Approach (3 page limit)*****E.1. Controls***

Describe your project management approach and what control mechanism you will put in place to track progress. This should include an organizational chart showing the relationships between the Principal Investigator and other team members.

***E.2. Risk Management***

Describe your overall risk mitigation strategy.

Provide an initial risk table. This table should include a list of project risks, an estimation of the severity of the risk (High,Medium,Low), and a brief risk mitigation approach for that risk.

***E.3. Subcontractor Management***

Describe management controls to be put in place for Subcontractor management if Subcontractors are a part of the proposed team.

**F. Appendix (no page limit)**

The Appendix section should be used for any additional information that the Offeror believes would be of valuable for the reviewers. Use this section for complete CVs of the team. An index of documents in the Appendix is required.

## **Attachment 3: Cost (or Price) Proposal Information Requirements**

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## Cost (or Price) Proposal Information Requirements

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Proposals which include unrealistic or unreasonable costs may be viewed as a failure to comprehend the complexity of the technical requirements. Proposals shall therefore demonstrate a complete understanding of the requirements and the associated complexities. Failure to adequately demonstrate this understanding and establish realistic costs accordingly may result in a failure to be further considered for award.

Information requested in this attachment is considered to be minimal and further information may be required prior to award of any Agreement.

### Specific Considerations:

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## Subcontract Cost (or Price) Proposal Information

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### A. Section One – Cost (or Price) Proposal

The cost (or price) proposal shall contain sufficient information to allow SAIC-F to perform an analysis of the proposed cost (or price) for the required deliverables. This information shall include the amounts of the basic elements of the proposed cost (or price) including, but not limited to, labor hour rates, travel, materials, Subcontracts.

In preparing your cost (or price) proposal, the following shall be considered:

- Offeror is to prepare their cost (or price) proposal using the Cost Proposal Worksheet provided as an attachment to this RFP and submitted with Offer in Microsoft Excel format.
- **Cost shall be broken out by deliverable and based on the number of fully-qualified cases the offeror believes they could provide to the CPTAC BCR in one calendar year.**
- In performance of the work, Offerors are expected to attend one CPTAC annual meeting as well as the following teleconference meetings (Travel costs shall be listed separate from deliverable costs.):
  - Kick-Off Meeting
  - Monthly Project Team Meeting
  - Monthly CPTAC TSS Program Meeting.
- Offerors shall provide substantive detail regarding the cost (or price) proposed so as to enable reviewers to objectively determine the reasonableness. Failure to provide a level of detail to facilitate this determination may result in the proposal being considered nonresponsive.

**B. Section Two – Cost (or Price) Justification and Documentation**

In this section, provide justifications and explanations of the proposed costs. This INCLUDES explanation of the processes by which extended costs were derived and a basis for why the proposed costs should be considered reasonable. The supporting information to be provided includes, but is not limited to:

- Labor costs. Provide labor categories and descriptions, if the proposed positions have not been filled or are to be named or hired, provide description of anticipated position and estimated labor category and rate.
- Demonstration of the reasonableness of any proposed consultant or lower-tier Subcontractor consulting costs, including demonstration that the proposed rates/costs are in keeping with those normally charged for the work to be performed.

# CPTAC Cost Proposal Templates Provided As Separate Document

## **Attachment 4: Certificate of Accounting and Billing System Adequacy**

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## Certificate of Accounting and Billing System Adequacy

Offeror Instructions: If none of the criteria in Section I applies, complete Section II – otherwise, proceed to Section III.

### Section I – Approved System(s)

Mark "X" in the appropriate column and provide information requested:	Accounting	Billing	Both
Defense Contract Audit Agency (DCAA) audit report No. _____ dated _____ as evidenced by the enclosed report.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Defense Contract Management Agency (DCMA) audit dated _____ as approved by the enclosed letter No. _____ dated _____.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other Government Agency audit dated _____ as approved by the enclosed letter No. _____ dated _____.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

### Section II—Evaluation Checklist

If Offeror selects "No" or "N/A" for any of the following questions, Offeror must provide an explanation under Section III – Offeror Remarks for each instance whereby one of these selections is made.

Mark "X" in the appropriate column. (If "N/A" or "No," explain in remarks section below.)	Yes	No	N/A
1. Is the accounting system in accordance with generally accepted accounting principles applicable in the circumstances?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Accounting system provides for:			

Mark "X" in the appropriate column. (If "N/A" or "No," explain in remarks section below.)		Yes	No	N/A
a.	Proper segregation of direct costs from indirect costs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b.	Identification and accumulation of direct costs by contract.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c.	A logical and consistent method for the allocation of indirect costs to intermediate and final cost objectives. (A contract is a final cost objective.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d.	Accumulation of costs under general ledger control.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e.	A timekeeping system that identifies employees' labor by intermediate or final cost objectives.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f.	A labor distribution system that charges direct and indirect labor to appropriate cost objectives.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
g.	Monthly accounting of Subcontract costs incurred.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
h.	Exclusion from costs charged to Government contracts of amounts which are not allowable in terms of Federal Acquisition Regulation (FAR) 31, Contract Cost Principles and Procedures, or other contract provisions.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i.	Identification of costs by contract line item and by units (as if each unit or line item were a separate contract) if required by the proposed contract.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
j.	Segregation of preproduction costs from production costs.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.	Accounting system provides financial information:			

Mark "X" in the appropriate column. (If "N/A" or "No," explain in remarks section below.)	Yes	No	N/A
a. Required by contract clauses concerning limitation of cost (FAR 52.232-20 and 21) or limitation on payments (FAR 52.216-16).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Required to support requests for progress payments.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Is the accounting system designed, and are the records maintained in such a manner that adequate, reliable data are developed for use in pricing follow-on acquisitions?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Is the accounting system currently in full operation? (If not, describe in the narrative which portions are (1) in operation, (2) set up but not yet in operation, (3) anticipated, or (4) nonexistent.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Billing system allows for:			
a. Segregation and exclusion of unallowable costs as required by FAR or Defense Federal Acquisition Supplement (DFARS)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b. Timely notification to prime contractor of overpayments/underpayments.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Segregation of incurred costs that may be non-billable because the costs may not meet specified criteria	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d. Adjusting submissions for final rates or indirect billing rates that differ from the billed rates	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e. Identifies costs that require specific approvals (special purchases, overtime authorizations, etc.).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Mark "X" in the appropriate column. (If "N/A" or "No," explain in remarks section below.)	Yes	No	N/A
f. Identifying contract overpayments, making refunds in a timely manner, and offsetting contract overpayments against contract underpayments.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

**Section III—Offeror Remarks:**

The undersigned attests to the accuracy of the foregoing and agrees to promptly notify SAIC-Frederick, Inc. (SAIC-F) of any changes to its Accounting, Billing System, and/or related internal control structure that would affect its ability to report hours delivered accurately and completely, and bill costs according to FAR Part 31, Contract Cost Principles and Procedures.

**Company Name:** \_\_\_\_\_

**Name of Signator:** \_\_\_\_\_

**Signature:** \_\_\_\_\_

**Title:** \_\_\_\_\_

**Telephone Number:** \_\_\_\_\_

**Date of Execution:** \_\_\_\_\_

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This Section to be Completed by SAIC-F

**Section IV—SAIC-F Contracting Officer Review/Approval**

Name of Signator:

Signature:

Title:

Date of Execution:

Recommendation:

**Section V—SAIC-F Internal Audit Review/Approval**

Name of Signator:

Signature:

Title:

Date of Execution:

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**Recommendation:**

<b>Action</b>	<b>Yes</b>	<b>No</b>	<b>N/A</b>
Corrective Action Plan Received?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Audit Conducted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>