

Request For Quotation (RFQ) Number: N02C054417-02

TOTAL 100% SMALL BUSINESS SET-ASIDE

Tissue Purchase Order Acquisitions for NCI's

Clinical Proteomic Tumor Analysis Consortium (CPTAC)

Response Due Dates (assuming an RFQ issue date of 7/30/15)

The **final** due date and time for submission of quotations received in response to this RFQ is **December 17, 2015 at 3:00pm (eastern prevailing time)**. All responses submitted by the below **interim closing** due dates/times will be evaluated and award decisions will be made based upon the information contained in this RFQ. Offerors are permitted to submit responses at any time; provided that all responses are received by the last due date and time specified within this RFQ. Responses received after the final due date and time may not be considered. The Government reserves the right to change the interim and final due dates/times by amendment to this RFQ. If adequate responses are received to accomplish the goals of CPTAC, NCI reserves the right to cancel any remaining interim closing dates at any time. If adequate responses are not received, NCI shall continue the response cut-off dates and change the final closing date. The Government intends to start making awards after the first interim closing date and awards will continually be made based upon submissions received by the below due dates.

Below are the anticipated due dates and times for submission of responses:

Interim Closing Due Dates/Times (subject to change)

August 13, 2015 at 3:00pm (eastern prevailing time)
August 27, 2015 at 3:00pm (eastern prevailing time)
September 10, 2015 at 3:00pm (eastern prevailing time)
September 24, 2015 at 3:00pm (eastern prevailing time)
October 8, 2015 at 3:00pm (eastern prevailing time)
October 22, 2015 at 3:00pm (eastern prevailing time)
November 5, 2015 at 3:00pm (eastern prevailing time)
November 19, 2015 at 3:00pm (eastern prevailing time)
December 3, 2015 at 3:00pm (eastern prevailing time)

Final Closing Date and Time (subject to change)

December 17, 2015 at 3:00pm (eastern prevailing time)

Responses or questions concerning this RFQ should be sent electronically to: Contracting Officers, Mandie S. White at whitem@mailto.nih.gov and C. Timothy Crilley at tcrilley@mailto.nih.gov. Please place the RFQ number in the subject line of your email.

1 Background and Introduction

The National Cancer Institute is expanding its basic and translational research programs that rely heavily on sufficient availability of high quality, well annotated biospecimens suitable for use in genomic and proteomic studies. The NCI's overarching goal with such programs is to improve the ability to diagnose, treat, and prevent cancer.

The overall objective of the Clinical Proteomic Tumor Analysis Consortium (CPTAC) is to improve our understanding of cancer biology by conducting proteogenomic analysis on selected cancer types (up to 10 cancer types, 200 cases each) where unanswered questions remain about the molecular biology of the disease. For this project, a case includes a tumor, adjacent normal tissue, and a source of germline DNA, such as blood. This analysis will add a complementary layer of protein molecular biology that facilitates the refinement of driver genes, enhances the understanding of the pathogenesis through proteomic subtyping, and illuminates the mechanism of dysregulation of cancer signaling networks and pathways via dynamic alterations in posttranslational modifications. To successfully generate comprehensive data, CPTAC will need in excess of 3,000 cases over the course of the project. This number assumes 2000 qualified cases with a 55% qualification rate.

The Contractor shall provide clinically annotated biospecimens from among the identified cancer types listed in Appendix B to CPTAC.

2 Statement of Work for CPTAC Biospecimens

To meet CPTAC goals, NCI will award multiple indefinite delivery/indefinite quantity commercial item purchase order awards to organizations (Contractors) that will deliver clinically annotated biospecimens. The tissues and non-clinical data will be delivered to one of CPTAC's Biospecimen Core Resource(s) (BCR) for storage, quality control, processing into molecular analytes, and other research efforts. Clinical data shall be supplied to the Comprehensive Data Resource (CDR). The histological specifications and annotation requirements of the cancers to be studied by CPTAC, the number of cases and biospecimens required per cancer, and preferred timing for their delivery to a BCR will be specified within each individual delivery order issued under the indefinite delivery/indefinite quantity purchase order.

In performance of this purchase order, the Contractor shall ensure that:

- All biospecimens and data (other than Case Report Forms [CRFs]) must be shipped directly from the contractor to a CPTAC BCR. The Government will identify the BCR

responsible for receiving the biospecimens and data and will provide this information to the contractor prior to packaging and shipping of the biospecimens.

- The logistics and protocols governing transfer of biospecimens and data from the contractor to BCR will be directed by the BCR assigned to receive materials from that particular contractor.
- This purchase order is for biospecimens obtained from predominantly prospective protocols, provided that the biospecimens and data meet CPTAC specifications. If retrospectively collected biospecimens meet the CPTAC requirements as shown by documentation are available, these biospecimens may be submitted after obtaining specific approval from the NCI Contracting Officer's Representative (COR). It is anticipated that the majority of biospecimens will be predominantly prospectively obtained and, therefore, these purchase order awards are largely worded as such. If however, the contractor already has retrospective material collected under the same or similar protocols as would be used prospectively for this work, such biospecimens and data may be delivered under this SOW upon receiving explicit approval from the NCI COR.

2.1 Requirements for Policies, Biospecimens and Data.

NCI and the National Institutes of Health (NIH) have established a number of policy and technical requirements that must be adhered to by contractors contributing biospecimens to CPTAC.

2.1.1 CPTAC policy requirements

The following administrative and policy requirements must be inherent in all relationships resulting in delivery of annotated biospecimens for CPTAC.

2.1.1.1 NCI site visit of tissue source sites

The contractor must provide to the NCI COR the names of Institutional Review Board (IRB) approved protocols obtaining biospecimens at those sites for delivery to CPTAC. NCI reserves the right to perform site visits to the contractor's site under the following terms:

- Site visits will be with reasonable notice and scheduling to accommodate all parties.
- Site visits will be for the purpose of auditing the contractor's compliance with CPTAC, NCI and NIH policies, and/or with the contractor's own protocols provided to NCI for this work. If the contractor is not in compliance with CPTAC, NCI or NIH policies, and/or with the contractor's own protocols provided to NCI for this work, the Government is not obligated to issue any delivery orders to the contractor and may terminate any current delivery orders.

2.1.1.2 Communication

- Kick Off
 - An initial kick off meeting will be held via teleconference within ten (10) calendar days of award or as agreed to by the NCI COR and Contracting Officer. The NCI COR, Key Contractor personnel, the Office of Acquisition's Contract Specialist and/or Contracting Officer, as well as the representative(s) from the Contractor's 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 Contractor shall be prepared to discuss the following:
 - Technical objectives.
 - Deliverables and deliverable acceptance criteria.
 - Reporting and invoice requirements.
- Monthly CPTAC Tissue Collection Team Meeting
 - A monthly teleconference will be held amongst the Tissue Source Sites, the NCI COR, and the CPTAC BCRs. The NCI COR will oversee the meeting. The purpose of the meeting is to review the progress on the biospecimen collection, update the Contractor on the latest program status, disseminate any protocol updates, and ensure open and ongoing communication amongst all the stakeholders and participants in the tissue procurement activities.
- CPTAC Semi-Annual Meeting
 - The Contractor is invited to attend the CPTAC Semi-Annual Meeting. The tentative location of the annual meeting is in the Washington, D.C. metro area. Attendance is not required. If the Contractor attends, the costs incurred for attending these meetings are not reimbursable under the respective purchase order(s) and shall be paid for by the Contractor.

2.1.1.3 Institutional Review Board (IRB) review, IRB protocol and Informed Consent

For all biospecimens and data submitted under this CPTAC purchase order award, the contractor shall provide written documentation to NCI that an IRB has reviewed and approved participation. Such approval includes the cases when an IRB does not consider the work to be human subjects research (e.g. if participants are deceased) or considers the work to be exempt – documentation of these IRB positions is still required.

In addition, the contractor must adhere to the following informed consent requirements:

- Patients must give, or have given, informed consent for collection of the cancer and normal samples with genetic, genomic, and/or proteomic research being specifically permitted.
- The contractor shall provide documentation of donor-specific date of consent and/or date of death for all cases.

In the case of new prospective collection protocols initiated in support of this work, the contractor shall provide copies of IRB protocols, IRB approvals, and the currently in use informed consent form.

2.1.1.4 Data Use Agreement

Biospecimens and data must be provided to CPTAC under a Data Use Agreement that is in compliance with Health Insurance Portability and Accountability Act (HIPAA) Limited Data Set requirements (as of September 2009). Additionally, biospecimens and data must be provided without any requirements for delayed use, delayed publication, review, or periods of data exclusivity for any party, with respect to the biospecimens and data provided or to the research data resulting from use of the biospecimens and data. Should applicable HIPAA regulations be modified over the term of this work, the Contractor shall make necessary changes in the subject contract(s) and Standard Operating Procedures (SOPs) to remain in compliance.

2.1.1.5 No automatic guest authorship

Biospecimens and data provided to CPTAC must be free of any automatic requirement to include investigators or other staff as authors on publications, merely by virtue of those individuals being CPTAC tissue and data providers.

2.1.1.6 Intellectual Property

Biospecimens and associated data must be provided to CPTAC free of any intellectual property encumbrances. Contractor Intellectual Property rights will be governed exclusively by FAR 52.227-14, Rights in Data –General and the terms stated within this Statement of Work.

2.1.1.7 Material Transfer Agreement

Many of the above requirements of this policy section are embedded in Material Transfer Agreements (MTA). The contractor shall enter into an MTA with at least one of CPTAC's BCRs, and the MTA must meet the following requirements:

- A copy of the executed MTA, with signatures, shall be given to NCI to be deposited in CPTAC's document repository.
- The NCI is not a party to the MTA.

- The MTA terms shall include the following:
 - MATERIAL shall be defined to include both the physical biospecimens and the associated annotation data.
 - MATERIAL is for research use only, i.e., not for treatment, transplant, or diagnosis.
 - All parties shall comply with relevant laws.
 - PROVIDER does not retain intellectual property reach through rights to datasets generated with MATERIALS or DERIVATIVES or to future discoveries arising from those datasets.
 - Terms shall not differentiate between nonprofit and for-profit entities being part of CPTAC's operations or data generating networks.
 - Terms shall not differentiate between nonprofit and for-profit entity access to datasets.
 - RECIPIENT is the custodian of the MATERIAL and acquires no ownership or intellectual property rights in the MATERIAL, derivatives, or future discoveries.
 - At the end of the project, MATERIAL and derivatives shall be disposed of under the direction of the NCI.
 - MTA shall pre-authorize the BCR to redistribute MATERIAL and DERIVATIVES to the various centers associated with CPTAC.
- Regarding associated annotation data, MTA terms shall include:
 - A requirement that incoming data from the contractor 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.
 - 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 Centers (DCC/CDR) under an appropriate Data Use Agreement (DUA).
- MTA shall require that the RECIPIENT not attempt to identify or contact MATERIAL donor or family members.

A template MTA for use in providing materials to a CPTAC BCR is provided in Appendix A.

2.1.2 Specification of Cancers to be Collected

The contractor shall provide cancer biospecimens, including, but not limited to, those provided in Appendix B. This list is preliminary, and is subject to having cancers added or eliminated. NCI may elect to approve the collection and banking of cancers not currently on the list.

NCI will make available to the Contractor the overall project objectives in terms of cancers to be studied and the general timelines for collection. This general information

will be made available for information purposes only and shall not be used to begin significant cost-incurring operations for annotated biospecimen accrual for CPTAC. This general information will be made available by providing contractor information from the relevant CPTAC Steering Committee and sub-committee working groups from which CPTAC planning and decision making occur.

2.1.3 Biospecimen Requirements

The Contractor shall provide the following to NCI before the tissue samples are shipped to the BCR:

- Draft detailed Criteria for acquisition of biospecimens, including:
 - Physical and biological characteristics of tissues.
 - Number and timing of delivery of biospecimens required by CPTAC.
 - A list of cancer specific data elements that must accompany each case's set of biospecimens.
- The Contractor shall initially draft the above Criteria for each cancer. These draft Criteria shall be submitted to NCI for review and approval, and possible modification. If Criteria for a particular cancer type have already been developed by NCI, they will be provided to the Contractor. Draft criteria shall be due from the Contractor within fifteen (15) calendar days of notification from NCI that a particular cancer type collection should begin. The Contractor should note that some cancers will be initiated at time of issuance of the delivery order, and others will start later in CPTAC's schedule.
- NCI shall approve the final Criteria (which may vary by cancer type) which shall then be adopted by Contractor for biospecimen accrual.
- All biospecimens shall be collected in a kit sent by a CPTAC BCR. The Contractor shall order kits from the BCR based on the number of biospecimens to be collected.
- Shipping -
 - Shipping will be arranged by a CPTAC BCR. The CPTAC BCR will provide the shipping container and pay for the costs of shipping.
 - Except for extraordinary circumstance preauthorized by the NCI COR, individual shipments will be arranged for the tissues obtained from a minimum of six (6) or more cases.
 - Each case shall include a completed Submission Case Report Form containing details regarding procurement such as times, tissue weights, etc., along with minimal patient information.

The following sections describe the default criteria for CPTAC biospecimens. The default criteria may change during the course of CPTAC based upon scientific or technology changes. Such change management shall be addressed via the section entitled, "Changes to Biospecimen Criteria" (below).

2.1.3.1 Biospecimen Criteria for CPTAC

The contractor shall provide per-case biospecimen sets that meet the following criteria:

- Both tumor tissue, normal adjacent tissue, and a source of germline DNA (blood or component, DNA, and/or adjacent normal tissue) samples must be available for every case. For some tumor types, normal adjacent tissue may not be available. Tumor types with this exception are listed in Appendix B
- Primary tumor samples:
 - Derived from patients with a primary, untreated malignancy.
 - Snap-frozen in liquid nitrogen vapor phase.
 - Sufficient tissue to yield a minimum of 1000 ug of protein and 20 ug of co-isolated DNA and RNA (depending on the extraction efficiency from tissue materials for their molecular contents, it is estimated to be approximately 200 – 250 mg wet tissue without OCT or other additives).
 - Secondary tumors are excluded.
 - Optionally, neoadjuvantly treated recurrent tumors and/or metastases are requested, but only when case-matched with a primary, untreated specimen is available.
 - The time from cutoff of in vivo blood supply (devascularization) to ex vivo stabilization (freezing) must be within 30 minutes; however 15 minutes or less is preferred. For all cases, this total ischemic time must be documented.
 - A case-matched representative FFPE H&E section, or whole slide H&E stained digital image of section, from the original anatomic pathology diagnostic block of the tumor, confirmatory of the cancer.
 - Cellular composition of tumor sample must be known or able to be determined. By default for any cancer, the following tissue cellular composition cutoff values should be use. Note, however, that cancer-specific values are subject to change at the discretion of the NCI, as dictated by CPTAC goals and technological requirements.
 - Each tumor sample will be composed predominantly of histologically viable appearing tumor cells
 - Of viable cell nuclei present, on average, $\geq 80\%$ should be tumor nuclei.
 - $\leq 20\%$ of viable cells present may be normal stromal, inflammatory or immune cells
 - The requirements below relate to sample volume and area of the histological slide.
 - If necrosis is present, it may comprise no more than 20% of the total sample area of the histological slide.
 - Of the total sample area of the histological slide, at least 50% must be comprised of viable cells (tumor or otherwise, not extracellular matrix).
- Normal tissue and blood:

- Blood or blood component, a frozen sample of normal tissue, or both from the same patient must be available for each case for purpose of obtaining germline DNA. In order of preference, the following are suitable: whole blood, PBL, purified DNA, other normal solid tissue.
- The sample must be sufficient to yield at least 20 micrograms of DNA and RNA.
- The normal adjacent tissue sample must be sufficient to yield at least 500 micrograms of protein.
- The normal adjacent tissue sample shall be snap frozen in liquid nitrogen vapor phase within 35 minutes of the cut off of in vivo blood supply (devascularization).
- If previously extracted DNA is provided, 20 micrograms should be prepared. Assuming a normal white blood cell count and optimal cell recovery techniques, one 10-ml tube of blood is sufficient for the recovery of 20µg of DNA, the optimal amount for CPTAC analyses. If the white count is low or the cell recovery techniques are sub-optimal, more blood may be required. Collection tube types, in descending order of preference are:
 - Yellow-top tube (Becton-Dickinson CPT, sodium citrate)
 - Blue-top tube (Sodium citrate)
 - Green-top tube (Heparin based tube)
 - Purple-top tube (EDTA) or red/black tiger-top tube (EDTA)
- Tumor biospecimens must be prescreened by the contractor to meet CPTAC specifications. Prescreening shall be performed on two sections taken directly adjacent to opposing surfaces of the frozen candidate sample that would be sent to BCR. Any samples containing tumor within 10% of the cutoff value shall be submitted, as determined by review of a single section from one surface of the frozen material. Standard Operating Protocols for this process are in Appendix C.

2.1.3.2 Changes to Biospecimen Criteria

Cancer-specific biospecimen requirements shall be developed over the course of CPTAC, and will result in deviation from the above defaults. These deviations may not be known at the time of issuance of the purchase order award and/or individual delivery orders. Currently known deviations are listed by cancer in Appendix D. As such changes become established by the NCI over the course of the project, the RFQ will be amended to include these changes. As this project develops over time, there may be changes to the quantities, delivery schedule, tumor types, CPTAC program management, shipping and reporting requirements, etc. If such changes occur, they will be communicated to the awardees.

2.1.4 Clinical and Other Data Delivery Requirements

2.1.4.1 Data requirements for CPTAC

For each CPTAC case of biospecimens provided to CPTAC, the following data shall be provided:

- Original surgical pathology report, appropriately de-identified, to be submitted with the specimens.
- Biospecimen case control form, to be submitted with the specimens, which includes the documentation of informed consent and/or date of death.
- Biospecimen submission case report form, which includes data about the biospecimen collection (such as total ischemic time) to ensure its eligibility for qualification shall be submitted with the specimen.
- Baseline and Supplemental Case Report Forms (CRF) data, to be submitted to the Comprehensive Data Resource (CDR) once BCR has notified the contractor that the specimens have passed relevant Quality Control steps.
 - To receive Payment 3, 100% of data elements are required.
 - Data must be delivered within thirty (30) calendar days of BCR notification
- Follow-up / outcomes CRF at 12 month intervals, until either the patient is deceased or the term of the award.
- Example CPTAC generic and cancer-specific data collection forms are in Appendix E.

2.2 Payment Schedule for Biospecimens and Data and Other Applicable Information

1. A case is defined as all of the components identified in Payments 1 – 4. For CPTAC designated cases, NCI will make fractional payments on the total per case price according to the following milestones:
 - Payment 1 (40% of total fixed price per case): Upon enrollment of the participant; banking of the tissue specimens; histological pre-screen of primary tumor specimen; delivery of tumor and normal specimens to BCR; and delivery of surgical pathology report and case control forms to BCR. The number of samples that fail the quality control step at the BCR is limited to 50% of the total samples contracted for a specific tumor type. Once a site reaches this threshold for a specific tumor type, any future cases that fail quality control for that tumor type will not receive a payment #1. Instead, additional cases can be submitted and samples that pass quality control can qualify for payments 2-4.
 - Payment 2 (30% of total fixed price per case): Upon the case's biospecimens passing BCR pathology and molecular Quality Control (QC) steps. The Government will only pay for samples that pass QC.
 - Payment 3 (15% of total fixed price per case): Upon delivery of Enrollment, Follow-Up (if available) and Supplemental data case report forms to CDR within 30 calendar

days of being notified that a case's biospecimens have passed BCR QC. Contractors will be required to provide a refund or replacement case at the discretion of the COR, at no cost to the Government if these data cannot be provided within 6 months after receipt of the request. A formalin fixed paraffin embedded (FFPE) slide or images from the FFPE diagnostic block shall be submitted at this time for all qualifying cases.

- Payment 4 (15% of total fixed price per case): Payment to be paid at conclusion of contract period for receipt of clinical follow-up information collected at 1 year intervals or 4 months prior to a data freeze, whichever is sooner, or until patient is deceased. Total compensation is 15% for all follow-on clinical data.
- Payments 5 and 6: Additional completed Follow-Up data (see payment 4 for details) are requested from sites to improve the overall data on the CPTAC cohort. Additional annual follow-up forms with related treatment data can garner additional follow-up payments, deemed payments 5 and 6 (for example, depending upon the receipt of sample(s), groups could provide one in 2015 and one in 2016). Additional Payments 5 and 6 may be offered, when funding remains available, to sites for those samples that have already provided approved data equivalent to that described in payment 4. At one year intervals, sites can coordinate with the NCI COR to provide additional follow-up data on still living patients or patients that have died since the prior follow-up/treatment forms were submitted to the CDR. Payments 5 and 6 are hereby added in an effort to replace payments that were not previously utilized for payments 1, 2, 3 or 4 either due to no delivery or cases that did not pass QC.
- Recurrent and Metastatic Specimens: An additional payment of 20% of total fixed price per case will be made for recurrent and metastatic specimens and data case-matched to the samples provided in Payment 1 above. Such samples shall only be provided upon specific request from NCI.
- All deliverables and correspondence must be in English.
- NCI will contact the contractor with regards to the Material Transfer Agreement(s) between the contractor and the BCR.

2. The following FAR and HHSAR clauses are applicable to the purchase orders:

- FAR 52.212-4, Contract Terms and Conditions – Commercial Items (May 2015)
- FAR 52.212-5, Contract Terms and Conditions Required to Implement Statutes or Executive Orders – Commercial Items (May 2015)
- FAR 52.215-2, Audit and Records – Negotiation (October 2010 with Alternate I (March 2009)
- HHSAR 352.223-70 Safety and Health
- FAR 52.227-14 Rights in Data – General (May 2014)
- FAR 52.216-18, Ordering (Oct 1995)
- FAR 52.216-19, Order Limitations (October 1995)
- FAR 52.216-22, Indefinite Quantity (Oct 1995)
- FAR 52.217-6, Option for Increased Quantity (Mar 1989)
- FAR 52.217-7, Option for Increased Quantity-Separately Priced Line Item (Mar 1989)

- FAR 52.217-8, Option to Extend Services (Nov 1999)
- FAR 52.217-9, Option to Extend the Term of the Contract (March 2000)
- HHSAR 352.224-70 (January 2006), Privacy Act
- FAR 52.224-1, Privacy Act Notification (April 1984)
- FAR 52.224-2, Privacy Act (April 1984)
- FAR 52.243-1, Changes – Fixed – Price (August 1987)
- 52.232-18, Availability of Funds (April 1984)
- HHSAR 352.239-71, Standard for Encryption (January 2010)
- HHSAR 352.239-73(b), Electronic and Information Technology Accessibility (Jan 2010)

The following 508 standards shall be employed:

- 1194.21 Software Applications and Operating Systems
- 1194.22 Web-Based Internet Information and Applications
- 1194.31 Functional Performance Criteria
- 1194.41 Information, Documentation and Support

3. Each purchase order awarded will include the following:

- The Privacy Act may be applicable and if so, a Privacy Act System of Records will be incorporated into all resulting purchase orders. See Appendix G, System of Records Number 09-25-0200.

- **Confidential Treatment of Sensitive Information**

The Contractor shall guarantee strict confidentiality of the information/data that is requested by the Government or that is provided to the Government during the performance of the contract. The Government has determined that the information/data that is requested by the Government or that the Contractor will be provided during the performance of the contract is of a sensitive nature.

Disclosure of the information/data, in whole or in part, by the Contractor can only be made after the Contractor receives prior written approval from the Contracting Officer. Whenever the Contractor is uncertain with regard to the proper handling of information/data under the contract, the Contractor shall obtain a written determination from the Contracting Officer.

- HHSAR 352.223-70 Safety and Health, FAR 52.227-14 Rights in Data – General, FAR 52.212-4 Contract Terms and Conditions – Commercial Items, FAR 52.212-5 Contract Terms and Conditions Required to Implement Statutes or Executive Orders – Commercial Items

- It is hereby understood and agreed that research involving human subjects shall not be conducted under this contract, and that no material developed, modified, or delivered by or to the Government under this contract, or any subsequent modification of such material, will be used by the Contractor or made available by the Contractor for use by anyone other than the Government, for experimental or therapeutic use involving humans without the prior written approval of the Contracting Officer.

3 Firm Fixed Price Proposal and Award Information

This RFQ is for delivering biospecimen sets at a fixed price per case for a case that successfully meets the clinical, pathological and data requirements of CPTAC. A case is defined as all of the components identified in Payments 1 – 6 (see Section 2.2.). Therefore, cases must be proposed on a total fixed price per case per cancer type for this RFQ, NCI will make payments of fractions of that fixed price upon milestone events that mirror the main cost-incurring stages of biospecimen and data collection, review, and distribution to CPTAC.

Offerors may propose on all, some, or only one cancer type stated within this RFQ. Offerors may submit more than one response on all, some or only one cancer type stated within this RFQ.

Based upon CPTAC programmatic priorities, the Government reserves the right to award a portion or up to all of the tissue types or quantities proposed. That is, any amount, any cancer tissue type, at any time at the Government's discretion.

Variable price (i.e., "cost +") proposals will not be considered.

3.1 Period of Performance and Other Information

This Request for Quotation (RFQ) is to solicit responses from organizations that can provide clinically annotated biospecimens to CPTAC in accordance with the Statement of Work.

The Government intends to award multiple indefinite delivery/indefinite quantity (ID/IQ) purchase orders with varying periods of performance and in varying quantities, depending upon the quantity and availability of the tissues proposed.

The period of performance for purchase orders may be less than or equal to 12 months and may or may not include options. The total period for each purchase order shall not exceed five (5) years. The government reserves the right to establish a period of performance for each individual purchase order based upon the information and number of samples proposed.

The following FAR clauses are applicable to this RFQ:

(reference below Section 6 – Full Text of FAR Clauses for the full text of most of these clauses. See <https://www.acquisition.gov/far/index.html> for full text of the Federal Acquisition Regulations):

- FAR 52.212-1, Instructions to Offerors – Commercial Items (April 2014)
- FAR 52.212-3, Offeror Representations and Certifications – Commercial Items (March 2015)

4 The minimum quantity awarded will be Payment 1 for one (1) sample.

5 The purchase order type is firm fixed price.

The Government may place firm fixed price delivery/task orders against an IDIQ contract in an amount not more than the minimum or maximum for the base year and each optional quantity as follows:

The Contractor shall be reimbursed by the Government in an amount not less than a total of the minimum commitment nor more than a total of the maximum commitment as stated on the SF1449 Form, for the base period and each option of performance.

All sales of the Contractor's products and services to the Government shall be made at such prices and on such terms as the Contract establishes at the time the order is placed. When purchasing such products or services, pricing shall be according to the current commercial price for the tissue and data in which the delivery order is being placed.

6 Basis for Award

Responses will be reviewed against the below technical criteria. The Government will be using a Pass/Fail approach; whereas, responses must meet all of the below criteria in order to be eligible for award. Although price is a significant factor, technical factors are equally as important as price to support a best value trade-off. Once an offeror has been determined to be technically acceptable, the Government will award according to price. The Government reserves the right to make awards resulting from this solicitation to the responsible offerors whose offer is the most advantageous to the Government, price and other factors considered.

- Provide evidence of a projected collection of at least 15 cases of a targeted cancer type or across targeted cancer types (Appendix B).
- Provide evidence that all tumors are primary and untreated.
- Provide a reasonable plan for how the samples will be snap frozen in vapor phase of liquid nitrogen or colder and stored under nitrogen vapor.

- Provide the protocol for resection of tissue and provide evidence that the time from devascularization to freezing is no longer than 30 minutes.
- Provide an appropriate plan for collecting a case-matched representative FFPE hemotoxylin and eosin (H&E) section, or whole slide H&E stained digital image of the section from the original anatomic pathology diagnostic block of the tumor.
- Provide a reasonable plan to pre-screen samples, which ensures cellular composition of tumor samples (i.e. percent tumor cellularity and necrosis) of greater than or equal to 70% tumor nuclei, less than 30% necrosis, and greater than 40% total cellularity.
- Provide a reasonable plan for ensuring that all tumor samples will have a matched normal control sample sufficient to yield at least 500 micrograms of protein and 20 micrograms of DNA (or 20 micrograms of DNA previously extracted DNA from case-matched normal tissue).
- Provide an appropriate plan for pre-screening samples.
- Provide evidence that original, de-identified pathology report is available for each case.
- Provide evidence that IRB approval is completed or is pending (i.e. provide a copy of the IRB document or proof of IRB pending status).
- Provide evidence that clinical data is available for each case.
- Provide a reasonable plan for ensuring that all tumor samples will be of sufficient size to yield at least 1000 micrograms of protein and 20 micrograms of DNA.
- Offeror must demonstrate acceptable past performance by providing evidence of successful biospecimen accrual for specialized collections not only for their organization, but for all key personnel, including the PI, officers, and executives.

7 To be Submitted with Offeror's Proposal

- Price per case of biospecimens, inclusive of all indirect costs.
- Supporting documentation for the price per case (i.e. commercial price list).
- For each cancer type (or sample) proposed, Offerors should specify the approximate date (within 1 month) when the samples will be ready to be shipped to the BCR.
- A list of proposed tumor types and for each:
 - the number expected to ship to the BCR;
 - the number expected to qualify at the BCR and;
 - the number expected to receive enrollment and 1 year follow-up CRFs.
- A RFQ response page limit of 20 pages, inclusive of all/any attachments.

8 Purchase Order Clauses and Terms

The following FAR clauses and Terms are applicable and will be incorporated in purchase orders. The below FAR clauses are being provided in full text (See <https://www.acquisition.gov/far/index.html> for full text of the Federal Acquisition Regulations):

- **FAR Clause 52.215-2, Audit and Records – Negotiation (OCTOBER 2010) with Alternate I (March 2009)**

(a) As used in this clause, “records” includes books, documents, accounting procedures and practices, and other data, regardless of type and regardless of whether such items are in written form, in the form of computer data, or in any other form.

(b) **Examination of costs.** If this is a cost-reimbursement, incentive, time-and-materials, labor-hour, or price redeterminable contract, or any combination of these, the Contractor shall maintain and the Contracting Officer, or an authorized representative of the Contracting Officer, shall have the right to examine and audit all records and other evidence sufficient to reflect properly all costs claimed to have been incurred or anticipated to be incurred directly or indirectly in performance of this contract. This right of examination shall include inspection at all reasonable times of the Contractor’s plants, or parts of them, engaged in performing the contract.

(c) **Certified cost or pricing data.** If the Contractor has been required to submit certified cost or pricing data in connection with any pricing action relating to this contract, the Contracting Officer, or an authorized representative of the Contracting Officer, in order to evaluate the accuracy, completeness, and currency of the certified cost or pricing data, shall have the right to examine and audit all of the Contractor’s records, including computations and projections, related to-

- (1) The proposal for the contract, subcontract, or modification;
- (2) The discussions conducted on the proposal(s), including those related to negotiating;
- (3) Pricing of the contract, subcontract, or modification; or
- (4) Performance of the contract, subcontract or modification.

(d) Comptroller General.-

(1) The Comptroller General of the United States, or an authorized representative, shall have access to and the right to examine any of the Contractor’s directly pertinent records involving transactions related to this contract or a subcontract hereunder and to interview any current employee regarding such transactions.

(2) This paragraph may not be construed to require the Contractor or subcontractor to create or maintain any record that the Contractor or subcontractor does not maintain in the ordinary course of business or pursuant to a provision of law.

(e) **Reports.** If the Contractor is required to furnish cost, funding, or performance reports, the Contracting Officer or an authorized representative of the Contracting Officer shall have the right to examine and audit the supporting records and materials, for the purpose of evaluating-

- (1) The effectiveness of the Contractor’s policies and procedures to produce data compatible with the objectives of these reports; and
- (2) The data reported.

(f) **Availability.** The Contractor shall make available at its office at all reasonable times the records, materials, and other evidence described in paragraphs (a), (b), (c), (d), and (e) of this clause, for examination, audit, or reproduction, until 3 years after final payment under this contract or for any shorter period specified in [Subpart 4.7](#),

Contractor Records Retention, of the Federal Acquisition Regulation (FAR), or for any longer period required by statute or by other clauses of this contract. In addition-

(1) If this contract is completely or partially terminated, the Contractor shall make available the records relating to the work terminated until 3 years after any resulting final termination settlement; and

(2) The Contractor shall make available records relating to appeals under the Disputes clause or to litigation or the settlement of claims arising under or relating to this contract until such appeals, litigation, or claims are finally resolved.

(g) The Contractor shall insert a clause containing all the terms of this clause, including this paragraph (g), in all subcontracts under this contract that exceed the simplified acquisition threshold, and-

(1) That are cost-reimbursement, incentive, time-and-materials, labor-hour, or price-redeterminable type or any combination of these;

(2) For which certified cost or pricing data are required; or

(3) That requires the subcontractor to furnish reports as discussed in paragraph (e) of this clause.

The clause may be altered only as necessary to identify properly the contracting parties and the Contracting Officer under the Government prime contract.

- **ORDERING AND ORDERING LIMITATIONS clauses**

- (1) **FAR 52.216-18 Ordering (Oct 1995)**

- (a) Any supplies and services to be furnished under this contract shall be ordered by issuance of delivery orders or task orders by the individuals or activities designated in the Schedule. Such orders may be issued from twelve (12) months from date of award.

- (b) All delivery orders or task orders are subject to the terms and conditions of this contract. In the event of conflict between a delivery order or task order and this contract, the contract shall control.

- (c) If mailed, a delivery order or task order is considered "issued" when the Government deposits the order in the mail. Orders may be issued orally, by facsimile, or by electronic commerce methods only if authorized in the Schedule.

As noted in FAR 52.216-18 Ordering (a), delivery orders or task orders will be processed by the following designated individuals, no other individuals are authorized Information:

To be determined at award

- (2) **FAR 52.216-19 Order Limitations (Oct. 1995)**

- (a) *Minimum order.* When the Government requires supplies or services covered by this contract in an amount of less than minimum quantity stated, the Government is not obligated to purchase, nor is the Contractor obligated to furnish, those

supplies or services under the contract.

(b) *Maximum order.* The Contractor is not obligated to honor—

- (1) Any order for a single item in excess of the maximum quantity stated;
- (2) Any order for a combination of items in excess of the maximum quantity stated;

Or

- (3) A series of orders from the same ordering office within 30 days that together call for quantities exceeding the limitation in paragraph (b)(1) or (2) of this section.

(c) If this is a requirements contract (i.e., includes the Requirements clause at subsection 52.216-21 of the Federal Acquisition Regulation (FAR)), the Government is not required to order a part of any one requirement from the Contractor if that requirement exceeds the maximum-order limitations in paragraph (b) of this section.

(d) Notwithstanding paragraphs (b) and (c) of this section, the Contractor shall honor any order exceeding the maximum order limitations in paragraph (b), unless that order (or orders) is returned to the ordering office within 10 calendar days after issuance, with written notice stating the Contractor's intent not to ship the item (or items) called for and the reasons. Upon receiving this notice, the Government may acquire the supplies or services from another source.

Note: The contractor shall NOT provide any service over the maximum quantity stated for the base year or each option year.

(3) FAR 52.216-22 Indefinite Quantity (Oct 1995)

- (a) This is an indefinite-quantity contract for the supplies or services specified and effective for the period stated, in the Schedule. The quantities of supplies and services specified in the Schedule are estimates only and are not purchased by this contract.
- (b) Delivery or performance shall be made only as authorized by orders issued in accordance with the Ordering clause. The Contractor shall furnish to the Government, when and if ordered, the supplies or services specified in the Schedule up to and including the quantity designated in the Schedule as the "maximum." The Government shall order at least the quantity of supplies or services designated in the Schedule as the "minimum."
- (c) Except for any limitations on quantities in the Order Limitations clause or in the Schedule, there is no limit on the number of orders that may be issued. The Government may issue orders requiring delivery to multiple destinations or performance at multiple locations.
- (d) Any order issued during the effective period of this contract and not

completed within that period shall be completed by the Contractor within the time specified in the order. The contract shall govern the Contractor's and Government's rights and obligations with respect to that order to the same extent as if the order were completed during the contract's effective period; provided that the Contractor shall not be required to make any deliveries under this contract after Period of Performance.

- **OPTIONS (to be included as applicable to each IDIQ Purchase Order Award)**

(1) FAR 52.217-6 Option for Increased Quantity (Mar 1989)

The Government may increase the quantity of supplies called for in the Schedule at the unit price specified. The Contracting Officer may exercise the option by written notice to the Contractor within one (1) calendar day. Delivery of the added items shall continue at the same rate as the like items called for under the contract, unless the parties otherwise agree.

(2) FAR 52.217-7 Option for Increased Quantity-Separately Priced Line Item (Mar 1989)

The Government may require the delivery of the numbered line item, identified in the Schedule as an option item, in the quantity and at the price stated in the Schedule. The Contracting Officer may exercise the option by written notice to the Contractor within one (1) calendar day. Delivery of added items shall continue at the same rate that like items are called for under the contract, unless the parties otherwise agree.

(3) FAR 52.217-8 Option to Extend Services (November 1999)

The Government may require continued performance of any services within the limits and at the rates specified in the contract. These rates may be adjusted only as a result of revisions to prevailing labor rates provided by the Secretary of Labor. The option provision may be exercised more than once, but the total extension of performance hereunder shall not exceed six (6) months. The Contracting Officer may exercise the option by written notice to the Contractor within one (1) calendar day.

(4) FAR 52.217-9 Option to Extend the Term of the Contract (March 2000)

- (a) The Government may extend the term of this contract by written notice to the Contractor within one (1) calendar day; provided that the Government gives the Contractor a preliminary written notice of its intent to extend at least one (1) calendar day before the contract expires. The preliminary notice does not commit the Government to an extension.
- (b) If the Government exercises this option, the extended contract shall be considered to include this option clause.

- (c) The total duration of this contract, including the exercise of any options under this clause, shall not exceed 60 months.

- **DELIVERY**

Deliveries and Acceptance:

Satisfactory performance of this award shall be deemed to occur upon the Contractor's delivery and acceptance by the Government. For the purpose of this award, the duly authorized representative, is the Contracting Officer's Representative. The Contracting Officer or the duly authorized representative will perform inspection and acceptance of materials and services to be provided. Inspection and acceptance shall be performed *at* the address of the duly authorized representative. Acceptance may be presumed unless otherwise indicated in writing by the Contracting Officer or duly authorized representative within 30 calendar days of delivery.

In accordance with Sections 2.1 (specifically, 2.1.3.1 and 2.1.4) and 2.2 of the Statement of Work, the below bullets constitute a complete case. In order to receive Payment 1, the contractor must meet the requirements of the Statement of Work in terms of delivery and acceptance and provide:

- Tumor sample
- Adjacent normal sample
- Blood
- De-identified surgical pathology report
- Biospecimen case control form

Monthly Status Reports

Acceptance of a Monthly Status Report shall initiate payment of a given case. Monthly Reports shall contain a list of all contracted tumor types and the number of cases in each of the stages listed below:

- Shipped to the BCR;
- Qualified at the BCR;
- Baseline CRFs submitted to the BCR;
- 12 month annual follow-up CRFs submitted to the BCR

Monthly Status Reports shall include a description of the activities completed during the reporting period and the activities planned for the ensuing reporting period. The first reporting period consists of the first full month of performance plus any fractional part of the initial month. Thereafter, the reporting period shall consist of each calendar month.

Monthly Status Report shall be due on or before the 30th calendar day following each reporting period and shall be sent electronically to the Contracting Officer and Contracting Officer's Representative.

Final Report

A Final Report is to include a summation of the work performed and results obtained for the entire contract period of performance to include, but not limited to the information contained in the monthly status reports. This report shall be in sufficient detail to describe comprehensively the results achieved. The Final Report shall be due on or before the expiration date of the IDIQ contract and shall be sent electronically to the Contracting Officer and Contracting Officer's Representative.

- **Contracting Officers Representative (COR)**

The COR is responsible for: (1) monitoring the Contractor's technical progress, including the surveillance and assessment of performance and recommended to the Contracting Officer changes in requirements; (2) interpreting the specifications and any other technical performance requirements; (3) performing technical evaluation as required; (4) performing technical inspections and acceptances required by this purchase order; and (5) assisting in the resolution of technical problems encountered during performance.

The Contracting Officer is the only person with authority to act as agent of the Government under this purchase order. Only the Contracting Officer has authority to: (1) direct or negotiate any changes in the specifications; (2) modify or extend the period of performance; (3) change the delivery schedule; (4) authorize reimbursement to the Contractor any costs incurred during the performance of this contract; or (5) otherwise change any terms and conditions of this contract.

The Government may unilaterally change its COR designation. COR information will be provided at award of contract.

- **INVOICE SUBMISSION**

Invoices shall be submitted in accordance with the below Invoice and Payment Provisions to the contract.

Invoice and Payment Provisions (2/2014)

The following clause is applicable to all Purchase Orders, Task or Delivery Orders, and Blanket Purchase Agreement (BPA) Calls: **Prompt Payment (Jul 2013) FAR 52.232-25**. Highlights of this clause and NIH implementation requirements follow:

I Invoice Requirements

- A. An invoice is the Contractor's bill or written request for payment under the contract for supplies delivered or services performed. A proper invoice is an "Original" which must include the items listed in subdivisions 1 through 12, below, in addition to the requirements of FAR 32.9. If the invoice does not comply with these requirements, the Contractor will be notified of the defect within 7 days after the date the designated billing office received the invoice (3 days for meat, meat food products, or fish, and 5 days for perishable agricultural commodities, dairy products, edible fats or oils) with a

statement of the reasons why it is not a proper invoice. (See exceptions under II., below.) Untimely notification will be taken into account in the computation of any interest penalty owed the Contractor.

1. Vendor/Contractor: Name, Address, Point of Contact for the invoice (Name, title, telephone number, e-mail and mailing address of point of contact).
2. Remit-to address (Name and complete mailing address to send payment).
3. Remittance name must match exactly with name on original order/contract. If the Remittance name differs from the Legal Business Name, then both names must appear on the invoice.
4. Invoice date.
5. Unique invoice #s for all invoices per vendor regardless of site.
6. NBS document number formats must be included for awards created in the NBS: Contract Number; Purchase Order Number; Task or Delivery Order Number and Source Award Number (e.g., Indefinite Delivery Contract number; General Services Administration number); or, BPA Call Number and BPA Parent Award Number.
7. Data Universal Numbering System (DUNS) or DUNS + 4 as registered in the Central Contractor Registration (CCR).
8. Federal Taxpayer Identification Number (TIN). In those exceptional cases where a contractor does not have a DUNS number or TIN, a Vendor Identification Number (VIN) must be referenced on the invoice. The VIN is the number that appears after the contractor's name on the face page of the award document.
9. Identify that payment is to be made using a three-way match.
10. Description of supplies/services **that match** the description on the award, by line billed.*
11. Freight or delivery charge must be billed as shown on the award. If it is included in the item price do not bill it separately. If identified in the award as a separate line item, it must be billed separately.
12. Quantity, Unit of Measure, Unit Price, Extended Price of supplies delivered or services performed, as applicable, and that **match** the line items specified in the award.*

* NOTE: If your invoice must differ from the line items on the award, please contact the Contracting Officer before submitting the invoice. A modification to the order or contract may be needed before the invoice can be submitted and paid.

- B. Shipping costs will be reimbursed only if authorized by the Contract/Purchase Order. If authorized, shipping costs must be itemized. Where shipping costs exceed \$100, the invoice must be supported by a bill of lading or a paid carrier's receipt.
- C. Mail an original and 1 copy of the itemized invoice to:

National Institutes of Health

Office of Financial Management,
Commercial Accounts
2115 East Jefferson Street, Room 4B-432,
MSC 8500
Bethesda, MD 20892-8500

For inquiries regarding payment call: (301) 496-6088

In order to facilitate the prompt payment of invoices, it is recommended that the vendor submit a photocopy of the invoice to the "Consignee" designated for the acquisition in blocks 6A – 6E of the face page of the Order/Award document.

II. Invoice Payment

- A. Except as indicated in paragraph B., below, the due date for making invoice payments by the designated payment office shall be the later of the following two events:
 - 1. The 30th day after the designated billing office has received a proper invoice.
 - 2. The 30th day after Government acceptance of supplies delivered or services performed.
- B. The due date for making invoice payments for meat and meat food products, perishable agricultural commodities, dairy products, and edible fats or oils, shall be in accordance with the Prompt Payment Act, as amended.

III. Interest Penalties

- A. An interest penalty shall be paid automatically, if payment is not made by the due date and the conditions listed below are met, if applicable.
 - 1. A proper invoice was received by the designated billing office.
 - 2. A receiving report or other Government documentation authorizing payment was processed and there was no disagreement over quantity, quality, or contractor compliance with a term or condition.
 - 3. In the case of a final invoice for any balance of funds due the contractor for supplies delivered or services performed, the amount was not subject to further settlement actions between the Government and the Contractor.

- B. Determination of interest and penalties due will be made in accordance with the provisions of the Prompt Payment Act, as amended, the Contract Disputes Act, and regulations issued by the Office of Management and Budget.

IV. PROVIDING ACCELERATED PAYMENT TO SMALL BUSINESS SUBCONTRACTORS, FAR 52.232-40 (December 2013)

- a. Upon receipt of accelerated payments from the Government, the Contractor shall make accelerated payments to its small business subcontractors under this contract, to the maximum extent practicable and prior to when such payment is otherwise required under the applicable contract or subcontract, after receipt of a proper invoice and all other required documentation from the small business subcontractor.
- b. The acceleration of payments under this clause does not provide any new rights under the prompt Payment Act.
- c. Include the substance of this clause, include this paragraph c, in all subcontracts with small business concerns, including subcontracts with small business concerns for the acquisition of commercial items.

(End of Clause)

Appendices

Appendix A: Material Transfer Agreement (template)

Appendix B: List of cancers

Appendix C: SOP for prescreen of biospecimens

Appendix D: Cancer-specific biospecimen composition deviations currently known

Appendix E: Data collection forms

Appendix F: Invoice Template (fixed-price)

Appendix G: Privacy Act System of Records (09-25-0200)

<http://oma.od.nih.gov/public/ms/privacy/pafiles/0200.htm>

Appendix A: Material Transfer Agreement template

The Clinical Proteomic Tumor Analysis Consortium (CPTAC) Material Transfer and Data Use Agreement

For Transfers to the CPTAC Biospecimen Core Resource (BCR) from organizations providing human biospecimens

This Agreement is by and between _____ <insert name of institution providing biospecimens > (“Provider”) and _____ <insert name of institution receiving biospecimens> (“Recipient”) regarding the transfer of human specimens and associated data to the Recipient as part of The Clinical Proteomic Tumor Analysis Consortium (CPTAC) project. Provider and Recipient are collectively referred to as the “Parties.”

WHEREAS, in order to improve the ability to diagnose, treat, and prevent cancer, the National Cancer Institute (“NCI”), a member institute of the National Institutes of Health, an agency of the federal government, have jointly undertaken the CPTAC -project as a comprehensive and coordinated research effort to accelerate the understanding of the molecular basis of cancer through the application of genome analysis technologies, including large-scale genome sequencing;

WHEREAS, the major organizational components of the CPTAC are the CPTAC Biospecimen Core Resource (“BCR”), the CPTAC Genome Characterization Centers, the CPTAC Proteogenomic Data Analysis Centers, the CPTAC Proteomic Translational Centers, the NCI-OTS contractors, the CPTAC Data Coordination Center (“DCC”), the CPTAC Quality Management System, and the CPTAC Proteome Characterization Centers, which are third party institutions funded by the NCI (collectively known as the “Centers”). ;

WHEREAS, the purpose of the CPTAC BCR is to minimize the variability introduced by the collection, processing and handling of selected human biospecimens and derivative materials that will be studied during the course of the CPTAC project;

WHEREAS, Provider, a covered entity subject to the Health Insurance Portability and Accountability Act of 1996, as amended, and accompanying regulations, intends to transfer a set of human biospecimens and associated data to Recipient;

WHEREAS, Recipient is funded to operate as the CPTAC BCR under a contract to receive, process and distribute human biospecimens, derivative materials and associated data to the CPTAC Centers;

WHEREAS, Recipient, will receive, process and distribute biospecimens received from Provider, materials derived from such biospecimens, and associated data to the CPTAC Centers;

WHEREAS, Provider and Recipient desire to protect the privacy and provide for the security of certain information disclosed to Recipient in compliance with HIPAA and other applicable laws and regulations,

NOW, THEREFORE, in consideration of the mutual promises in this Agreement and for other good and valuable consideration, the sufficiency of which is hereby acknowledged, the Parties hereby agree as follows:

1. **DEFINITIONS.** Within this Agreement, the following terms will have the same meaning as those used in the *Standards for Privacy of Individually Identifiable Health Information* set forth in 45 CFR Parts 160 and 164 (“HIPAA Privacy Rule. These terms are repeated here for convenience.

(a) Under 45 CFR 164.500 (“Applicability”), a “covered entity” is an organization, individual, institution, or other entity that is subject to the standards, requirements, and implementation specifications of the HIPAA Privacy Rule with respect to protected health information under.

(b) Under 45 CFR 164.514 (“Other requirements relating to uses and disclosures of protected health information”), “De-identified” information is information that formerly contained individually identifiable health information, but which has had all unique identifying information, numbers, characteristics, and codes removed such that the information a record contains cannot be used alone or in combination with other information to identify the individual who is the subject of the information. Identifying information includes, but is not limited to, the 18 categories of identifiers described in 45 CFR 164.514(b)(2).

(c) Under 45 CFR 164.501 (“Definitions”), “Protected Health Information” or “PHI” means any information, whether oral or recorded in any form or medium: (i) that relates to the past, present, or future physical or mental condition of an individual; the provision of health care to an individual; or the past, present, or future payment for the provision of health care to an individual, and (ii) that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

(d) Under 45 CFR 164.514(e) (“Implementation Specification: Limited data set”), a “limited data set” (herein “LDS”) is protected health information that excludes the 15 specific direct identifiers listed in that section. Any such identifying information that identifies the individual who is the subject of the PHI, his or her relatives, employers, or household members must be removed for the PHI to constitute an LDS. Unlike de-identified PHI, and LDS *may* contain postal address information, including a town, city, State, or zip code; specific dates, for example, dates of birth, admission, treatment, or release; and any other information, not specifically listed in that section, that could be used alone or in combination with other information to identify a specific individual.

2. DESCRIPTION OF MATERIAL AND DATA.

(a) The material to be transferred (“ORIGINAL MATERIAL”) is a set of human biospecimens described specifically as:

(b) The data to be transferred to Recipient are clinical, biological, technical or other information describing the ORIGINAL MATERIAL specimens (“DATA”). Some of the DATA may be PHI. DATA, regardless of whether or not it is PHI regulated by HIPAA, will be transferred in a form technically compliant with an LDS. The DATA may include the following data elements: dates; timestamps; ages; dates of birth, death, admission and discharge; dates of service; and geographical information, including zip codes or any other geographic subdivisions.

3. COLLECTION OF MATERIAL AND DATA. The ORIGINAL MATERIAL and DATA have been collected by Provider under an Institutional Review Board (“IRB”) approved protocol, including all necessary informed consents, and authorizations, which disclose potential redistributions of the ORIGINAL MATERIAL or materials derived from the ORIGINAL MATERIAL, e.g., DNA and RNA products (“DERIVATIVE MATERIAL”) (ORIGINAL and DERIVATIVE MATERIAL are collectively referred to as “MATERIAL”) and DATA, in accordance with Section 4 of this Agreement, in compliance with all applicable laws, regulations and policies for the protection of human subjects, including 45 CFR Part 46, “Protection of Human Subjects” (the “Common Rule”), the HIPAA Privacy Rule, and any necessary approvals, authorizations, human subjects assurances, informed consent documents, and IRB approvals.

4. TRANSFER OF ORIGINAL MATERIAL AND DATA; PURPOSE. Provider agrees to provide the ORIGINAL MATERIAL and DATA in accordance with applicable laws, regulations and policies, including the Common Rule, the HIPAA Privacy Rule, and any necessary authorizations, human subjects’ assurances, informed consent documents, and IRB approvals. Provider will remove any elements of the 15 LDS-specific direct identifiers from the DATA before transfer to Recipient. The sole purpose of the Provider’s transfer of the DATA to Recipient is to enable Recipient to receive, process and distribute the ORIGINAL and DERIVATIVE MATERIALS, and DATA to the CPTAC Centers in fulfillment of their obligations to the NCI.

(a) Provider hereby grants Recipient explicit permission to further distribute the MATERIAL and DE-IDENTIFIED DATA to the CPTAC Centers.

(b) Provider hereby grants Recipient explicit permission to further distribute the DATA to the CPTAC DCC located at the NCI upon execution between Recipient and NCI of a data use agreement that is consistent with the terms of this agreement. Furthermore, Provider acknowledges and agrees that Recipient may allow the CPTAC DCC to provide all or part of the DATA to third parties under separate data use agreements that are no less restrictive than this Agreement and that prohibits such third parties from further distributing the LDS.

5. RESPONSIBILITIES AND AUTHORIZATIONS OF RECIPIENT

(a) Recipient is authorized to receive the ORIGINAL MATERIAL AND DATA under an IRB approved protocol or IRB granted waiver. Recipient agrees to handle and distribute the MATERIAL in accordance with all applicable laws, regulations and policies, including, as applicable, the Common Rule, the HIPAA Privacy Rule, and any necessary human subject’s assurances, informed consents and IRB approvals.

(b) Recipient is not authorized and shall not further disclose the DATA other than as permitted by this Agreement or as otherwise required by law. Recipient shall not distribute the DATA to other third parties without written consent from Provider and NCI’s Contracting Officer.

(c) Recipient shall use appropriate administrative, technical, and physical safeguards to prevent use or disclosure of the DATA other than as provided for in this Agreement.

(d) Recipient shall notify Provider in writing within five (5) working days of its discovery of any use or disclosure of the DATA not permitted by this Agreement of which Recipient, its officers, employees, or agents become aware. Recipient shall take (i) prompt corrective action to cure any deficiencies or (ii) any action pertaining to such unauthorized disclosure required by applicable federal law.

(e) Recipient shall ensure that any of its agents or subcontractors agrees with Recipient in writing that such agent or subcontractor will hold any DATA transmitted from the Recipient to such agent or subcontractor confidential and will use or disclose the DATA only for the purpose for which it was used or disclosed to the agent or subcontractor, or as required by law. Additionally, the agent or subcontractor shall notify Recipient of any instances, of which it is aware, in which the Information has been used or disclosed inconsistent with this Agreement.

(f) Recipient agrees to not identify or contact any donor or living relative who is associated with the MATERIAL or any DATA received under this Agreement from Provider. Furthermore, Recipient will not attempt to obtain or otherwise acquire any DATA associated with the MATERIAL beyond that which is provided by the Provider.

(h) Recipient will retain and abide by this Agreement for as long as it retains DATA received from the Provider plus 6 (six) years after the date it returns or destroys all such information.

6. BREACH OR VIOLATION. Provider is not responsible for Recipient's violations of this Agreement, unless Provider knows of a pattern of activity or practice that constitutes a material breach or violation of this Agreement, in which case it must take reasonable steps to cure the breach, end the violation or withhold the DATA delivered to Recipient.

7. THE MATERIAL AND DATA ARE NOT FOR USE IN HUMAN SUBJECTS OR FOR THE TREATMENT OR DIAGNOSIS OF HUMAN SUBJECTS.

8. DISCLAIMER. Any MATERIAL delivered pursuant to this Agreement is understood to be experimental in nature and may have hazardous properties. SUBJECT TO THE REPRESENTATIONS IN SECTION THREE (3) ABOVE WITH RESPECT TO THE MATERIAL OR DATA, PROVIDER MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE MATERIAL OR DATA WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER PROPRIETARY RIGHTS. To the extent allowed by law, Recipient assumes liability for claims for damages against it by third parties which may arise from its use, storage, processing, distribution or disposal of the MATERIAL except that, to the extent permitted by law, Provider shall be liable to Recipient when the damage is caused by the gross negligence or willful misconduct of Provider.

9. DISPOSAL OF MATERIAL AND DATA. At the end of its contract with NCI, Recipient will dispose of the MATERIAL and DATA in the manner decided at the sole discretion of NCI and consistent with law and the informed consent of the individual providing the ORIGINAL MATERIAL. Such disposition on behalf of NCI may include, but is not limited to, continued storage on behalf of NCI for future research, return to Provider, transfer to the NCI, use in an expansion of CPTAC, transfer to another organization acting on NCI's behalf, or destruction.

10. INTELLECTUAL PROPERTY. Provider acknowledges and agrees that it does not by virtue of this Agreement acquire any intellectual property rights in the future inventions or discoveries made by third parties using the MATERIAL or DATA distributed by Recipient. Recipient acknowledges that it serves only as the custodian of the MATERIAL and DATA, and therefore agrees that it does not by virtue of this Agreement acquire any intellectual property rights in the MATERIAL, nor any future intellectual property rights in any research conducted by third-parties using the MATERIAL or DATA.

Appendix B: List of Cancers

Sites	Misc. Info.
Glioblastoma multiforme	Normal adjacent tissue not required
Lung squamous cell carcinoma	
Pancreatic ductal adenocarcinoma	
Acute myeloid leukemia	Normal adjacent tissue is marrow from the patient in remission if available.
Clear Cell renal cell carcinoma	
Lung Adenocarcinoma	
Head and Neck squamous cell carcinoma	
Sarcoma	
Cutaneous melanoma	
Uterine corpus endometrial carcinoma	Normal adjacent tissue is normal uterine epithelium. This may not be available for all cases.

Appendix C – SOP for TSS Prescreen of biospecimens before shipment to BCR

TSS Preparation of Top Slides Working Instructions

I. Purpose:

The purpose of this instruction is to establish a procedure for obtaining a section of unfixed frozen tissue for a “top” slide.

Frozen tumor samples are submitted by the contractor to the Biospecimen Core Resource (BCR) for consideration in CPTAC. Prior to submission of those tissues the contractor creates one top slide and stains the slide with hemotoxylin and eosin. Each top slide is reviewed by a board certified pathologist at the TSS to evaluate tissue samples for submission to the BCR that meet inclusion requirements as evaluated by the pre-defined pathology qualification acceptance criteria for the project.

To ensure inclusion requirements contribution into the CPTAC project verify the following sample qualifying criteria are met:

- Both tumor and normal samples are available;
- Tumor sample size: ≥ 200 mg in weight;
- Adjacent normal tissue size: >50 mg in weight;
- Tumor samples will be comprised of $\geq 80\%$ tumor nuclei;
- The tumor tissue is comprised of $\leq 20\%$ necrosis ($\leq 50\%$ necrosis for GBM);
- Of the total area of the histological slide, at least 50% must be comprised of viable cells (tumor or otherwise);
- The adjacent normal tissue is comprised of 0% tumor nuclei and $\geq 50\%$ total cellularity;
- Tumor samples must be snap frozen (preferably in a cryo-cooler) and derived from patients with a primary, untreated malignancy;
- A frozen sample of normal tissue/blood from the same patient must be available for each case. Extracted DNA (minimum of 20 μ g) from patient blood or other normal tissue sample is also acceptable;
- Cellular composition of tumor sample is known or can be determined.
- Access to associated sample clinical data is available.

II. Procedure:

1. Ensure all utensils have been cleaned with 70% ethanol prior to placing in the cryostat and/or dry ice container.
2. Carefully remove frozen tissue samples from the storage cryofreezer and immediately transfer the sample(s) to a container of dry ice that is large enough to allow all samples to be kept completely frozen during the procedure of obtaining ‘top’ slides. **Ensure that the samples are kept cold with dry ice at all times.** If the

frozen tissue sample is not on dry ice, it must be inside a cryostat, a -80°C freezer or a cryofreezer.

3. Carefully remove the sample from its container with sterilized forceps and place it in a pre-chilled Petri dish on dry ice. When extracting the frozen tissue sample from its container, take extra care not to force the forceps through the container or tissue sample.

It is imperative that the tissue sample not be exposed to conditions that would promote thawing during this procedure.

4. **Be certain that the cryostat hand-wheel is in the locked position.** The frozen tissue sample, in the pre-chilled Petri dish on dry ice, will be transferred to a weigh boat using sterilized forceps. The weigh boat containing the frozen tissue sample will be immediately placed in the cryostat. Place an appropriate amount of OCT mounting medium on to the specimen disc and adhere the frozen tissue sample to the liquid OCT. Work quickly to ensure the tissue contains OCT before the medium freezes.
5. After the OCT has solidified, place the specimen disc onto the specimen head of the cryostat and tighten. Adjust the angle of the specimen head to ensure that a complete represented section of tissue will be obtained for the 'top' slide.
6. Place a clean, disposable blade into the blade holder and tighten.
7. Using proper cutting technique (refer to the cryostat manufacturer's microtomy procedure) face into the frozen tissue to expose the surface.
8. Obtain a 4 - 5 micron section and place on a blue glass slide. Blue slides represent 'top' to the BCR, however, any color of slide that is available to the TSS is acceptable. Ensure that the slide is properly labeled (using a Statmark pen) with the TSS unique patient identifier, (if applicable) the slide procurement date (e.g., 18 Jan 08) and the word 'top'.
9. **Be certain that the cryostat hand-wheel is in the locked position.** Remove the specimen disc from the specimen head of the microtome and place upside down (i.e. tissue facing down) in the dry ice.
10. To remove the frozen tissue from the "specimen disc", grip the base of the OCT with sterilized serrated tip forceps and twist for a clean breakaway of the frozen tissue sample containing OCT.
11. After the frozen tissue sample containing OCT is separated from the specimen disc, obtain a pre-chilled sample container that is large enough to allow space for the frozen tissue sample to be placed into it with the attached OCT surrounding it. A list of these sample containers include but are not limited to:
 - Plastic contact lens cases that have been snapped in half,
 - Aluminum foil,
 - Plastic embedding molds,
 - Tissue cassettes,
 - 50ml conical tubes,
 - Cryovials – ensuring OCT is NOT surrounding frozen tissue sample.

12. **At no time should the frozen tissue sample containing OCT be subjected to thawing conditions in order to fit into a sample container. A sample container must be obtained that will allow for the size of the frozen tissue sample with the OCT attached to fit into and maintain its original shape.**
13. Ensure that the TSS sample identification number is clearly visible on the sample container. Materials for TSS sample identification writing include: using a Sharpie® on tape to attach to the aluminum foil or for labeling the plastic contact lens cases and using a Statmark pen or pencil for labeling tissue cassettes, conical tubes or cryovials. Ensure that any label that is used for the purpose of the CPTAC project is capable of withstanding the extreme temperatures associated with a cryofreezer, a -80°C freezer, a cryostat or a cryoport.
14. Place frozen tissue sample containing OCT in a labeled sample container on dry ice large enough to accommodate a cardboard box for sample shipping.
15. Clean all utensils with 70% ethanol prior to starting new frozen tissue sample.
16. Obtain a new sterile Petri dish for the next frozen tissue sample. The used Petri dish must be discarded in the biohazard waste.
17. Obtain a new weigh boat for the next frozen tissue sample. The used weigh boat must be discarded in the biohazard waste.
18. Obtain a new blade for sectioning the next frozen tissue sample 'top' slide on the cryostat. Discard the used blade into a biohazard sharps container.
19. It is recommended for optimum quality control that a second person match the TSS number of the sample to the number on the sample container and to verify that the correct number is on the 'top' slide. These steps should be performed prior to H & E staining.
20. Once all the frozen tissue samples that have been sectioned for the 'top' slide are placed into their appropriate sample containers (i.e. the container that the frozen tissue sample will be shipped to the BCR in) and are in the cardboard storage box, it is necessary to then place the box of samples into a cryofreezer for storage until shipment to the BCR.
21. Stain 'top' slides using hematoxylin and eosin.
22. If a frozen tissue sample is in more than one piece and is from the same patient and tumor, it is imperative that the pieces be identified separately by being placed into individual sample containers and has a 'top' slide sectioned to represent each piece. If the TSS chooses to place the pieces into the same sample container for shipping to the BCR, each individual frozen tissue piece must be oriented with a small dab of tissue marking ink to assist the BCR on which end of the frozen tissue sample the section came from. Alternatively, you may aggregate the frozen tissue pieces and embed them together in OCT to obtain one representative section from all the tissue pieces.

III. Safety:

- Wear personal protective equipment (PPE) such as lab coats, nitrile or latex gloves, and eye goggles or face shield and close-toed shoes.

- Blood borne pathogens can be present in the unfixed frozen tissue, use universal precautions.
- Liquid nitrogen is extremely cold and can cause 'burns'. Wear gloves that are specially made to withstand liquid nitrogen, eye protection and a lab coat to protect skin from splashes and spills. Liquid nitrogen is an asphyxiant; be sure to use in a well-ventilated area.

IV. References: Equipment, Materials and Quality Control

Equipment and Materials:

- Cryostat
- Specimen discs compatible with the cryostats in use at the TSS.
- Optimal Cutting Temperature Medium (OCT, Lung Tissue Media-020108926)
- Shandon low profile microtome blades
- Serrated tip forceps (Fisher Scientific, Cat # 1381214)
- 100 mm sterile Petri dishes or tissue culture dishes (Falcon, or similar)
- Dry ice
- 1 insulated bucket for dry ice (Styrofoam or plastic)
- Frozen tumor tissue
- 4x4 gauze
- Nitrile/Latex gloves
- 70% Ethanol
- Blue frosted glass slides (Unimark)
- Statmark pen for slide identification (Cat # SMP-BK)
- Cardboard box specific for storage of cryovials and/or tissue samples

It is possible to substitute materials and certain equipment from other vendors as long as they are the equivalent of the item described above.

Products and disposable materials used need to be RNase-free, and handled only with gloved hands in order to prevent contamination with skin RNases.

All reagents must be made with RNase-free materials and chemicals, and containers and tubes with samples must be kept covered when possible during the entire procedure to ensure they remain dust and RNase-free. In the case that a reagent or disposable becomes contaminated, it must be discarded.

Quality Control:

- The frozen tissue sample must remain frozen throughout the entire procedure of obtaining a 'top' slide for the BCR. To ensure this always work with frozen tissue samples either inside a cryostat or in a container of dry ice.

- For optimum quality control, it is recommended that each frozen tissue sample be handled in teams of two histologists; each individual being proactive in sample identification, labeling of slides with the sample identification number and returning of frozen tissue sample to the cryofreezer prior to shipping to the BCR.
- All sample labels should be visually inspected by both individuals to ensure that the sample is being placed in an appropriately labeled vial.
- The cryostat should be checked prior to beginning any work to make sure it is in good working order (i.e., able to rotate one full rotation).
- Avoid tissue loss during the sectioning procedure. When creating sections, face the frozen tissue sample that is within OCT, removing only the quantity of tissue required to expose the surface.

TSS Pathology Prescreen Review of Tissue Specimen Top Slide Working Instructions

I. Purpose

The purpose of this working instruction is to establish a procedure for the Pathologist at the Tissue Source Site (TSS) to review biospecimen H&E slides and document pathology results. This procedure applies to all board-certified Pathologists as well as a board-certified Pathologist with specialized training.

Frozen tumor samples are submitted by the contractor to the Biospecimen Core Resource for consideration in CPTAC. Prior to submission of those tissues the contractor creates one top slide, one at either end of the tissue sample and stains the slide with hemotoxylin and eosin. Each top slide is reviewed by a board certified pathologist at the TSS to evaluate tissue samples for submission to the BCR that meet the qualification metrics as evaluated by the pre-defined pathology control acceptance criteria for the project (see Qualification Acceptance Criteria).

Working instructions do not supersede any Department Policies or Standard Operating Procedures; however, are intended for training and consistency of daily operational functions for CPTAC.

II. Procedure: Working Instruction Compilation and Maintenance

1. Review qualification acceptance criteria metrics for specimen consideration.
2. Document Tissue Source Site Tumor Slide Identifier on Case Quality Control Form.
3. Evaluate one newly created tumor specimen top H & E slide and one adjacent normal specimen top H&E slide per case utilizing appropriate pathology techniques to evaluate:

Confirmation of Diagnosis	Percent Necrosis*	Percent Tumor Nuclei*
<ul style="list-style-type: none"> • Glioblastoma Multiforme (GBM) 	$\leq 50\%$	$\geq 80\%$
<ul style="list-style-type: none"> • All other tumor types 	$\leq 20\%$	$\geq 70\%$
<ul style="list-style-type: none"> • Adjacent normal tissue 	$\leq 20\%$	<u>0%</u>
<ul style="list-style-type: none"> • *Note, submit specimens for evaluation within a 10% window of necrosis and nuclei metrics for consideration. 		

4. **Confirmation of Diagnosis:** The original case diagnosis (pathology report) should be compared and confirmed against the specimen slide under evaluation for project submission.
5. Document the confirmed diagnosis on the Case Quality Control Form.
6. **Percent Necrosis:** The entire specimen field should be evaluated under low power (2x-4x) magnification to determine the percent of tissue necrosis present utilizing geographical specimen landmarks as a measurement guide.
7. After initial estimation of necrosis, confirm percent estimate under high power (10x-40x) magnification to validate the absence of nuclei.
8. Document the percent necrosis on the Case Quality Control Form.
9. **Percent Tumor Nuclei:** A minimum of ten specimen fields should be evaluated under high power magnification. Begin at 10x and magnify up to 40x to evaluate the percentage of tumor nuclei within the viable non-necrotic specimen area to determine a quantitative percent representation of the number of tumor nuclei present.
10. Note: If homogenous consistency exists throughout the sample the pathologist must utilize professional judgment to increase the number of fields assessed to grade the percentage of tumor nuclei.
11. Document the percent tumor nuclei on the Case Quality Control Form.
12. It is important to note that pathology interpretation may vary; therefore once diagnosis is confirmed, it is acceptable to submit any specimen within a 10% window of calculation for evaluation. For example, if case evaluation returns 70% tumor nuclei submit case to the BCR for project consideration.
13. **Percent Total Cellularity:** Measure the area of the slide occupied by tissue (including cells, extracellular matrix, necrosis, etc.). This area is the denominator. Measure the area of the slide occupied by viable cells (tumor, normal, stroma, etc.). This area is the numerator. Divide the numerator by the denominator and multiply the quotient by 100%. The result is the percent total cellularity and shall be recorded on the Case Quality Control Form.

14. **Adjacent Normal Tissue:** For the adjacent normal tissue, a minimum of ten specimen fields should be evaluated under high power magnification. Begin at 10x and magnify up to 40x to evaluate the percentage of tumor nuclei within the viable non-necrotic specimen area to determine a quantitative percent representation of the number of tumor nuclei present. Tumor nuclei present in the adjacent normal tissue specimen will disqualify the specimen.
15. Document the percent tumor nuclei on the Case Quality Control Form.
16. Pathologist performing review signs Case Quality Control Form in section titled, "To Be Completed by Pathology."
17. Note: One form is to be completed per slide and submitted in plastic envelope with cryoport shipment to the BCR; see *Completion of Case Quality Control Form* instructions.
18. Prepare top slides for shipment to the BCR; see *Shipment of Top Slide* instructions.

III. Safety

1. Glass slides can have sharp edges. Be careful while handling any glass component.
2. Blood borne pathogens can be present in unfixed frozen tissue. Use universal personal protective equipment (PPE), such as lab coats and gloves when handling all specimens.

IV. References: Equipment, Materials and Quality Control

Equipment and Materials

- Light microscope
- H&E slide(s) of samples to be reviewed and documented
- Case Quality Control Form (*CPTAC #A1.034v2*)

Quality Control:

- Slide identifier should be verified against the slide number on CPTAC Quality Control Form when slide is placed on the microscope stage to ensure the correct slide is being reviewed.

Appendix D: Tumor cellular composition deviations from default currently known

Glioblastoma multiforme

Necrosis composition on prescreen section: qualifying sample is $\leq 50\%$

Appendix E: Data Collection Forms

See separately attached PDF documents - these forms are in the process of being drafted and shall be made available to the Contractor(s) prior to award.

Appendix F: Invoice Template (fixed-price)

To be provided with award documents.

Appendix G: Privacy Act System of Records

SORN #09-25-0200 <http://oma.od.nih.gov/public/ms/privacy/pafiles/0200.htm>