Request for Quotation (RFQ) Number: RFQ-NCI-10006-AS

Full and Open Competition

RECOVERY - Tissue Purchase Order Contract Acquisitions for NCI's

The Cancer Genome Atlas Program

Cancer Types: Glioblastoma multiforme, Lung squamous cell carcinoma, Breast ductal carcinoma, Colon adenocarcinoma, Breast lobular carcinoma, Lung Adenocarcinoma , Stomach adenocarcinoma, Other Cancer Types Currently Not Identified

Response Due Dates:

The **final** due date and time for submission of quotations received in response to this RFQ is **July 20, 2010 at 3:00pm (eastern prevailing time).** All responses submitted by the following **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 anytime; 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 will not be considered. The Government reserves the right to change the interim and final due dates/times by amendment to this RFQ. 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 due dates and times for submission of responses:

Interim Closing Due Dates/Times

December 18, 2009 at 3:00pm (eastern prevailing time)
January 4, 2010 at 3:00pm (eastern prevailing time)
January 18, 2010 at 3:00pm (eastern prevailing time)
February 1, 2010 at 3:00pm (eastern prevailing time)
February 16, 2010 at 3:00pm (eastern prevailing time)
March 2, 2010 at 3:00pm (eastern prevailing time)
March 16, 2010 at 3:00pm (eastern prevailing time)
March 30, 2010 at 3:00pm (eastern prevailing time)
April 13, 2010 at 3:00pm (eastern prevailing time)
April 27, 2010 at 3:00pm (eastern prevailing time)
May 11, 2010 at 3:00pm (eastern prevailing time)
May 25, 2010 at 3:00pm (eastern prevailing time)
June 8, 2010 at 3:00pm (eastern prevailing time)
June 22, 2010 at 3:00pm (eastern prevailing time)
July 6, 2010 at 3:00pm (eastern prevailing time)

Final Closing Date and Time
July 20, 2010 at 3:00pm (eastern prevailing time)

Responses should be sent electronically to the following individuals: Kim Goetz at goetzkm@mail.nih.gov; and Robin Irving at irvingr@mail.nih.gov.

Questions concerning this RFQ should be direct to the following individuals:

Kim Goetz, Contract Specialist, at 301/228-4225, goetzkm@mail.nih.gov
Robin M. Irving, Contracting Officer, at 301/228-4220, irvingr@mail.nih.gov

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 studies. The NCI's overarching goal with such programs is to improve the ability to diagnose, treat, and prevent cancer.

The Cancer Genome Atlas (TCGA), one such program, is a comprehensive and coordinated effort to accelerate our understanding of the molecular basis of cancer through the application of genome analysis technologies. The National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) launched TCGA as a 3-year pilot project in 2006, and have since (August 2009) initiated the second phase of the project to study at least 20 additional cancers over 5 years. This project aims to systematically explore the entire spectrum of genomic changes involved in human cancer. Specifically, the project is designed to comprehensively analyze DNA copy number changes, including large (on the order of chromosome segments) and small (1,000-100,000 kb) scale rearrangements, transcription profiles, epigenetic modifications, sequence variation, and sequence in both tumor tissue and case-matched germline DNA. The suite of analysis platforms will be applied to a common set of molecular analytes obtained from clinically annotated high-quality tumor biospecimens and case-matched normal tissue (control). More detailed information can be found at the project's website: http://cancergenome.nih.gov. To successfully generate comprehensive data in phase two, TCGA will need in excess of 40,000 biospecimens over course of the project.

The Contractor shall provide clinically annotated biospecimens to TCGA.

2 Statement of Work for TCGA Biospecimens

To meet TCGA goals, NCI will award multiple indefinite delivery/indefinite quantity commercial item purchase order contracts to organizations (Contractor) that will deliver clinically annotated biospecimens. The tissues and data will be delivered to one of TCGA's Biospecimen Core Resource(s) (BCR) for storage, quality control, processing into molecular analytes, and other research efforts. The histological specifications and annotation requirements of the cancers to be studied by TCGA, 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 contract.

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

- All biospecimens and data must be shipped directly from the contractor to a TCGA BCR, without transshipment through an intermediate site. The Government will identify the BCR responsible for receiving the biospecimens 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 contract is agnostic about whether clinically annotated cancer biospecimens are obtained from retrospective collections and/or from prospective protocols, provided that the biospecimens and data meet TCGA specifications. It is anticipated that the majority of biospecimens will be prospectively obtained and, therefore, this purchase order contract is largely worded as such; however, if 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. When both options are available, retrospective biospecimens are preferred so that samples are more quickly obtainable and outcomes data are more immediately available.

2.1 Requirements for Policies, Biospecimens and Data

NCI and NIH have established a number of policy and technical requirements that must be adhered to by contractors contributing biospecimens to TCGA.

2.1.1 TCGA policy requirements

The following administrative and policy requirements must be inherent in all relationships resulting in delivery of annotated biospecimen procurement for TCGA.

2.1.1.1 NCI site visit of tissue source sites

The contractor must provide to the NCI Contracting Officer's Representative (COR) the names of principle investigators on IRB-approved protocols obtaining biospecimens at those sites for delivery to TCGA. 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 parties.
- Site visits will be for the purpose of auditing the contractor' compliance with TCGA, NCI and NIH policies, and/or with the contractor' own protocols provided to NCI for this work. If the contractor is not in compliance with TCGA, 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 Institutional Review Board (IRB) review, IRB protocol and Informed Consent

For all biospecimens and data submitted under this TCGA purchase order contract, 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 and/or genomic 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.

2.1.1.3 Data Use Agreement

Biospecimens and data must be provided to TCGA under a Data Use Agreement that is in compliance with Health Insurance Portability and Accountability Act (HIPAA) Limited Data Set requirements (as of August 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, Contractor shall make necessary changes in contracts and Standard Operating Procedures (SOPs) to remain in compliance.

2.1.1.4 No automatic guest authorship

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

2.1.1.5 Intellectual Property

Biospecimens and associated data must be provided to TCGA 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.

2.1.1.6 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 one of TCGA'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 TCGA's document repository.
- The NCI is not 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 TCGA'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 TCGA.
- 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 TCGA Data Coordinating Centers (DCC) 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 TCGA 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 TCGA. This general information will be made available by providing contractor information from the relevant TCGA Steering Committee and sub-committee working groups on which TCGA 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 TCGA.
    - A list of cancer specific data elements that must accompany each case's set of biospecimens.

- The Contractor shall initially draft 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 Contractor within fifteen (15) calendar days of notification from NCI that a particular cancer's collection should begin. Contractor should note that some cancers will be initiated at time of issuance of the delivery order, and others will start later in TCGA's schedule.
- NCI shall approve the final Criteria (which may vary by cancer type) which shall then be adopted by Contractor for biospecimen accrual.

The following sections describe the default criteria for TCGA biospecimens. The default criteria may change during the course of TCGA based upon scientific or technology changes. Such change management shall be addressed in the project management plan (below).

2.1.3.1 Biospecimen Criteria for TCGA

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

- Both tumor tissue and a source of germline DNA (blood or component, DNA, and/or adjacent normal tissue) samples must be available for every case.
- Primary tumor samples:
    - Derived from patients with a primary, untreated malignancy.
    - Snap-frozen to -86 deg C or colder
    - Sufficient tissue to yield 20 ug of co-isolated DNA and RNA (this is typically 150 – 200 mg of tissue).
    - Secondary tumors are excluded.
    - Optionally, neoadjuvantly treated recurrent tumors and/or metastases are requested, but only when case-matched with a primary, untreated specimen.
    - The time from cutoff of in vivo blood supply (devascularization) to ex vivo stabilization (freezing) must be within 60 minutes; however 30 minutes or less is preferred.
    - 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 can 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 TCGA goals and technological requirements.
        - Each tumor sample will be composed predominantly of histologically viable appearing tumor cells

        - Of viable cell nuclei present, on average, >= 80% should be tumor nuclei.
        - <= 20% of viable cells present may be normal stromal, inflammatory or immune cells
        - If necrosis is present, it may comprise no more than 20% of sample volume.
- Normal tissue:
    - 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.
    - 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 recovery of 20-µg of DNA, the optimal amount for TCGA analyses. If the white count is low or the cell recovery techniques 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 TCGA specifications. Prescreening shall be performed on a single section taken directly adjacent to one surface 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.

Cancer-specific biospecimen requirements shall be developed over the course of TCGA, and will result in deviation from the above defaults. These deviations may not be known at the time of issuance of the purchase order contract 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. If such changes can reasonably be demonstrated by the Contractor to affect Contractor costs, NCI and Contractor will negotiate in good faith to modify the prices paid.

2.1.4 Clinical and other data delivery requirements

2.1.4.1 Data requirements for TCGA

For each TCGA case of biospecimens provided to TCGA, 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.
- Tier 1, Tier 2 and Supplemental Case Report Forms (CRF) data, to be submitted once BCR has notified the contractor that the specimens have passed relevant Quality Control steps.
    - For Tier 1: 100% of elements are required
    - For Tier 2 and Supplemental forms: >50% of form data elements are required for retrospective cases; 100% of form data elements are required for prospectively obtained cases.
    - Data must be delivered within sixty (60) calendar days of BCR notification
- Follow-up / outcomes CRF at 6 month intervals, until either the patient is deceased or the term of the contract.
- Current TCGA 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 TCGA designated cases, NCI will make fractional payments on the total per case price according to the following milestones:
    - Payment 1 (25% 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.
    - Payment 2 (25% 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 (25% of total fixed price per case): Upon delivery of Tier 1, Tier 2 and Supplemental data case report forms to BCR with 60 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 no cost to the Government if these data cannot be provided within 6 months after receipt of the request.
    - Payment 4 (25% of total fixed price per case): Payment to be paid at conclusion of contract period for receipt of clinical follow-up information collected at 6 month intervals or until patient is deceased. Total compensation is 25% for all follow-on clinical data.
    - 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.
2. The following FAR clauses are applicable to the purchase order contracts:

- 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
- FAR 52.204-11 – American Recovery and Reinvestment Act – Reporting Requirements (Mar 2009)
- FAR 52.203-15, Whistleblower Protections Under American Recovery and Reinvestment Act of 2009 (March 2009)
- FAR 52.215-2, Audit and Records – Negotiation (March 2009) with Alternate I (March 2009)
- HHSAR 352.223-70 Safety and Health
- FAR 52.227-14 Rights in Data – General
- FAR 52.216-18, Ordering (Oct 1995)
- FAR 52.216-19, Order Limitations (October 1995)
- FAR 52.216-22, Indefinite Quantity (Oct 1995)
- FAR 52.217-8, Option to Extend Services (Nov 1999)
- FAR 52.217-9, Option to Extend the Term of the Contract (March 2000)

3. Each purchase order contract 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 order contracts.

    - 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.

    - For purchase orders contracts funded with ARRA funds, the ARRA Reporting Requirements stated in Section 6 below will be incorporated in all ARRA funded purchase orders contracts and delivery orders.

    - 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 TCGA. A case is defined as all of the components identified in Payments 1 – 4 (see Section 2.2.). Therefore, while Offerors must propose total fixed price per case per cancer 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 TCGA.

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 TCGA programmatic priorities, the Government reserves the right to award a portion or up to all of the tissue types or quantities proposed.

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 TCGA in accordance with the Statement of Work.

The Government intends to award multiple indefinite delivery/indefinite quantity (ID/IQ) purchase order contracts with varying periods of performance and in varying quantities, depending upon the quantity and availability of the tissues proposed. The aggregate value of all purchase order contracts awarded under this RFQ will not exceed the commercial item ceiling of $5.5 million.

The period of performance for purchase order contracts may be less than or equal to 12 months and may or may not include options. The total period for each purchase order contract shall not exceed five (5) years. The government reserves the right to establish a period of

performance for each individual purchase order contract based upon the information and number of samples proposed by each offeror.

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
- FAR 52.212-3, Offeror Representations and Certifications

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

5 The purchase order type is firm fixed price.

6 Basis for Award

Responses will be reviewed against the following technical criteria. Responses must meet all of the below criteria in order to be eligible for award. Although price is a significant factor, technical factors are more important than 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.

- Describes a collection of at least 50 qualified cases of a targeted cancer type (Appendix B), or describes a collection of at least 500 qualified cases of another cancer type.
- Confirms that all tumors are primary and untreated.
- Describes how the samples were frozen at -86 deg C or colder and stored under nitrogen vapor.
- Describes the protocol for resection of tissue and confirms the time from devascularization to freezing is no longer than 60 minutes.
- Confirms existence of case-matched representative FFPE H&E section, or whole slide H&E stained digital image of the section from the original anatomic pathology diagnostic block of the tumor.
- Confirms cellular composition of tumor sample (i.e. percent tumor cellularity and necrosis) of ~70% tumor nuclei and less than 30% necrosis.
- Confirms that all tumor samples have a matched normal control sample sufficient to yield at least 20 micrograms of DNA (or 20 micrograms of DNA previously extracted DNA from case-matched normal tissue).
- Confirms samples have been pre-screened or describes a process for pre-screening.
- Confirms that original, de-identified pathology report is available for each case.

- Confirms IRB approval completed or is pending.
- Confirms that clinical data is available for each case.
- Reasonability of price per case

7 To be Submitted with Offeror's Proposal

- Price per case of biospecimens.
- 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 RFQ response page limit of 10 pages
- The Government intends to use ARRA funding for the purchase order contracts awarded under this RFQ. The offeror must clearly state, within its offer, their acceptance and agreement to comply with the ARRA provisions stated in this RFQ as these provisions will be incorporated in all ARRA funded purchase order contracts. If the offer does not clearly state agreement to comply with the ARRA terms, then award may be made using appropriated funds for these purchase order contracts, subject to availability of appropriated funds for these purchase orders contracts. The ARRA provisions are as follows:

Prior to processing the award, the contractor shall submit with his response confirmation from an officer of the company/organization that states that the company/organization will comply with the reporting requirements stated in Federal Acquisition clause 52.204-11. The reporting requirements are applicable to all contractors who receive ARRA funds. Those reporting requirements include:

1. The dollar amount of contractor invoices
2. The supplies delivered and services performed
3. An assessment of the completion status of the work
4. An estimate of the # of jobs created and retained
5. Names and total compensation of each of the five most highly compensated officers for the calendar year in which the contract is awarded; and
6. Specific information on first-tier subcontractors

The contractor shall confirm that the company/organization is aware of the Reporting Requirements and that the company/organization will comply with all Reporting Requirements. Below is a copy of the clause in full text.

52.204-11 – American Recovery and Reinvestment Act—Reporting Requirements (Mar 2009)

(a) *Definitions.* As used in this clause—

"Contract," as defined in FAR 2.101, means a mutually binding legal relationship obligating the seller to furnish the supplies or services (including construction) and the buyer to pay for them. It includes all types of commitments that obligate the Government to an expenditure of appropriated funds and that, except as otherwise authorized, are in writing. In addition to bilateral instruments, contracts include (but are not limited to) awards and notices of awards; job orders or task letters issued under basic ordering agreements; letter contracts; orders, such as contracts, under which the contract becomes effective by written acceptance or performance; and bilateral contract modifications. Contracts do not include grants and cooperative agreements covered by 31 U.S.C. 6301, *et seq*. For discussion of various types of contracts, see FAR Part 16.

"First-tier subcontract" means a subcontract awarded directly by a Federal Government prime contractor whose contract is funded by the Recovery Act.

"Jobs created" means an estimate of those new positions created and filled, or previously existing unfilled positions that are filled, as a result of funding by the American Recovery and Reinvestment Act of 2009 (Recovery Act). This definition covers only prime contractor positions established in the United States and outlying areas (see definition in FAR 2.101). The number shall be expressed as ''full-time equivalent'' (FTE), calculated cumulatively as all hours worked divided by the total number of hours in a full-time schedule, as defined by the contractor. For instance, two full-time employees and one part-time employee working half days would be reported as 2.5 FTE in each calendar quarter.

"Jobs retained" means an estimate of those previously existing filled positions that are retained as a result of funding by the American Recovery and Reinvestment Act of 2009 (Recovery Act). This definition covers only prime contractor positions established in the United States and outlying areas (see definition in FAR 2.101). The number shall be expressed as ''full-time equivalent'' (FTE), calculated cumulatively as all hours worked divided by the total number of hours in a full-time schedule, as defined by the contractor. For instance, two full-time employees and one part-time employee working half days would be reported as 2.5 FTE in each calendar quarter.

"Total compensation" means the cash and noncash dollar value earned by the executive during the contractor's past fiscal year of the following (for more information see 17 CFR 229.402(c)(2)):

(1) *Salary and bonus*.

(2) *Awards of stock, stock options, and stock appreciation rights*. Use the dollar amount recognized for financial statement reporting purposes with respect to the fiscal year in accordance with the Statement of Financial Accounting Standards No. 123 (Revised 2004) (FAS 123R), Shared Based Payments.

(3) *Earnings for services under non-equity incentive plans.* Does not include group life, health, hospitalization or medical reimbursement plans that do not discriminate in favor of executives, and are available generally to all salaried employees.

(4) *Change in pension value*. This is the change in present value of defined benefit and actuarial pension plans.

(5) *Above-market earnings on deferred compensation which is not tax-qualified*.

(6) *Other compensation*. For example, severance, termination payments, value of life insurance paid on behalf of the employee, perquisites or property if the value for the executive exceeds $10,000.

(b) This contract requires the contractor to provide products and/or services that are funded under the American Recovery and Reinvestment Act of 2009 (Recovery Act). Section 1512(c) of the Recovery Act requires each contractor to report on its use of Recovery Act funds under this contract. These reports will be made available to the public.

(c) Reports from contractors for all work funded, in whole or in part, by the Recovery Act, and for which an invoice is submitted prior to June 30, 2009, are due no later than July 10, 2009. Thereafter, reports shall be submitted no later than the 10th day after the end of each calendar quarter.

(d) The Contractor shall report the following information, using the online reporting tool available at *http://www.FederalReporting.gov* .

(1) The Government contract and order number, as applicable.

(2) The amount of Recovery Act funds invoiced by the contractor for the reporting period. A cumulative amount from all the reports submitted for this action will be maintained by the government's on-line reporting tool.

(3) A list of all significant services performed or supplies delivered, including construction, for which the contractor invoiced in this calendar quarter.

(4) Program or project title, if any.

(5) A description of the overall purpose and expected outcomes or results of the contract, including significant deliverables and, if appropriate, associated units of measure.

(6) An assessment of the contractor's progress towards the completion of the overall purpose and expected outcomes or results of the contract (i.e., not

started, less than 50 percent completed, completed 50 percent or more, or fully completed). This covers the contract (or portion thereof) funded by the Recovery Act.

(7) A narrative description of the employment impact of work funded by the Recovery Act. This narrative should be cumulative for each calendar quarter and only address the impact on the contractor's workforce. At a minimum, the contractor shall provide—

(i) A brief description of the types of jobs created and jobs retained in the United States and outlying areas (see definition in FAR 2.101). This description may rely on job titles, broader labor categories, or the contractor's existing practice for describing jobs as long as the terms used are widely understood and describe the general nature of the work; and

(ii) An estimate of the number of jobs created and jobs retained by the prime contractor, in the United States and outlying areas. A job cannot be reported as both created and retained.

(8) Names and total compensation of each of the five most highly compensated officers of the Contractor for the calendar year in which the contract is awarded if—

(i) In the Contractor's preceding fiscal year, the Contractor received—

(A) 80 percent or more of its annual gross revenues from Federal contracts (and subcontracts), loans, grants (and subgrants) and cooperative agreements; and

(B) $25,000,000 or more in annual gross revenues from Federal contracts (and subcontracts), loans, grants (and subgrants) and cooperative agreements; and

(ii) The public does not have access to information about the compensation of the senior executives through periodic reports filed under section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m(a), 78o(d)) or section 6104 of the Internal Revenue Code of 1986.

(9) For subcontracts valued at less than $25,000 or any subcontracts awarded to an individual, or subcontracts awarded to a subcontractor that in the previous tax year had gross income under $300,000, the Contractor shall only report the aggregate number of such first tier subcontracts awarded in the quarter and their aggregate total dollar amount.

(10) For any first-tier subcontract funded in whole or in part under the Recovery Act, that is over $25,000 and not subject to reporting under paragraph 9, the contractor shall require the subcontractor to provide the information described in (i), (ix), (x), and (xi) below to the contractor for the purposes of the quarterly report. The contractor shall advise the subcontractor that the information will be made available to the public as required by section 1512 of the Recovery Act. The contractor shall provide detailed information on these first-tier subcontracts as follows:

(i) Unique identifier (DUNS Number) for the subcontractor receiving the award and for the subcontractor's parent company, if the subcontractor has a parent company.

(ii) Name of the subcontractor.

(iii) Amount of the subcontract award.

(iv) Date of the subcontract award.

(v) The applicable North American Industry Classification System (NAICS) code.

(vi) Funding agency.

(vii) A description of the products or services (including construction) being provided under the subcontract, including the overall purpose and expected outcomes or results of the subcontract.

(viii) Subcontract number (the contract number assigned by the prime contractor).

(ix) Subcontractor's physical address including street address, city, state, and country. Also include the nine-digit zip code and congressional district if applicable.

(x) Subcontract primary performance location including street address, city, state, and country. Also include the nine-digit zip code *and congressional district if applicable.

(xi) Names and total compensation of each of the subcontractor's five most highly compensated officers, for the calendar year in which the subcontract is awarded if—

(A) In the subcontractor's preceding fiscal year, the subcontractor received—

(*1*) 80 percent or more of its annual gross revenues in Federal contracts (and subcontracts), loans, grants (and subgrants), and cooperative agreements; and

(*2*) $25,000,000 or more in annual gross revenues from Federal contracts (and subcontracts), loans, grants (and subgrants), and cooperative agreements; and

(B) The public does not have access to information about the compensation of the senior executives through periodic reports filed under section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m(a), 78o(d)) or section 6104 of the Internal Revenue Code of 1986

8 Purchase Order Clauses and Terms

The following FAR clauses and Terms are applicable and will be incorporated in purchase order contracts. 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 52.203-15, Whistleblower Protections Under the American Recovery and Reinvestment Act of 2009 (March 2009)**

  (a) The Contractor shall post notice of employees rights and remedies for whistleblower protections provided under section 1553 of the American Recovery and Reinvestment Act of 2009 (Pub.L. 111-5).

  (b) The Contractor shall include the substance of this clause including this paragraph (b) in all subcontracts. (End of Clause)

- **FAR Clause 52.215-2, Audit and Records – Negotiation (March 2009) with Alternate I (March 2009)**
- **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*, Phone: 301/ xxxx**
***To be determined*, Phone: 301/ xxxx**

(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 purchase order contract)**

(1) 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 thirty (30) days.

(2) FAR 52.217-9 Option of 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 30 calendar days; provided that the Government gives the Contractor a preliminary written notice of its intent to extend at least 30 calendar days 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 *** months.

- **DELIVERY**

Deliveries and Acceptance: Satisfactory performance of this contract shall be deemed to occur upon the Contractor's delivery and acceptance by the Government. For the purpose of this contract, 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.

- **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 it's COR designation: COR information will be provided at award of contract.

Name
Address
Bethesda, Maryland ***
(Phone) 301-xxxxxx

- **INVOICE SUBMISSION**

Invoices shall be submitted in accordance with Attachment I - INVOICE AND PAYMENT PROVISIONS to the contract.

Invoice and Payment Provisions (09/2008)

The following clause is applicable to all Purchase Orders, Task or Delivery Orders, and Blanket Purchase Agreement (BPA) Calls: ***Prompt Payment*** *(Oct 2003) 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. Invoices submitted for payment against awards made **on or after June 4, 2007**, must include the contractor's DUNS number and 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 one 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 for "Service Type Purchase Orders" e.g. Professional Services, Programming Services, it is recommended that the vendor submit a photocopy of the invoice to the Project Officer designated for the acquisition.

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.

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 A: Material Transfer Agreement template

The Cancer Genome Atlas Project (TCGA) Material Transfer and Data Use Agreement

For Transfers to the TCGA 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 Cancer Genome Atlas (TCGA) 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") and the National Human Genome Research Institute ("NHGRI"), member institutes of the National Institutes of Health, an agency of the federal government, have jointly undertaken the TCGA -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 TCGA are the TCGA Human Cancer Biospecimen Core Resource ("BCR"), the TCGA Genome Characterization Centers, the TCGA Genome Data Analysis Centers and TCGA Genome Sequencing Centers, which are third party institutions funded, respectively by the NCI and the NHGRI (collectively the "Centers"), and the TCGA Data Coordination Center ("DCC"), which is operated by NCI through the NCI Center for Bioinformatics;

WHEREAS, the purpose of the TCGA 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 TCGA 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 TCGA BCR under a contract to receive, process and distribute human biospecimens, derivative materials and associated data to the TCGA Centers;

WHEREAS, Recipient, will receive, process and distribute biospecimens received from Provider, materials derived from such biospecimens, and associated data to the TCGA 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 TCGA Centers and the TCGA DCC at NCI in fulfillment of its contractual obligations to NCI's OTS contractor ("Purpose").

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

(b) Provider hereby grants Recipient explicit permission to further distribute the DATA to the TCGA 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 TCGA 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 subjects 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 TCGA, 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.

SIGNATURES

_____ _____

Signing Official Date

_____

Name of institution providing biospecimens

_____ _____

Signing Official Date

_____

Name of institution receiving biospecimens

Appendix B: List of cancers

Sites
Glioblastoma multiforme
Lung squamous cell carcinoma
Breast ductal carcinoma
Colon adenocarcinoma
Breast lobular carcinoma
Lung Adenocarcinoma
Stomach adenocarcinoma
Other Cancer Types Currently Not Identified

Appendix C – SOP for TSS (Tissue Source Sites/Offeror Proposing Tissue) 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 TCGA. 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 inclusion requirements as evaluated by the pre-defined pathology qualification acceptance criteria for the project.

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

- Both tumor and normal samples are available;
- Tumor sample size: ≥200mg in weight;
- Tumor samples will be comprised of ≥ 80% tumor nuclei;
- The tissue is comprised of ≤ 20% necrosis (≤ 50% necrosis for GBM);
- Tumor samples must be snap frozen 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 13 µg) 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 dd 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 TCGA 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, eye goggles or face shield and close-toed shoes.
- Bloodborne 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

<u>Equipment and Materials:</u>

- 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.

<u>Quality Control</u>:

- 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 TCGA. 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 TCGA.

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 specimen top H & E slide per case utilizing appropriate pathology techniques to evaluate:

Confirmation of Diagnosis	Percent Necrosis*	Percent Tumor Nuclei*
• Glioblastoma Multiforme (GBM)	$\leq$ 50%	$\geq$ 80%
• Serous Cystadenocarcinoma	$\leq$ 20%	$\geq$ 70%

• Squamous Cell Carcinoma	≤ 20%	≥ 80%
*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 ~~TSS~~ 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. Pathologist performing review signs Case Quality Control Form in section titled, "To Be Completed by Pathology."
14. 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.
15. 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. Bloodborne 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 *(TCGA #A1.034v2)*

Quality Control:

- Slide identifier should be verified against the slide number on TCGA 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 >= 40%

Appendix E: Data collection forms

See separately attached PDF documents

File name: The Cancer Genome Atlas Forms – Lung.pdf

File name: The Cancer Genome Atlas Forms – Ovary.pdf

File name: The Cancer Genome Atlas Forms – GBM.pdf