OFFICE OF ACQUISITIONS
NATIONAL CANCER INSTITUTE

REQUEST FOR PROPOSAL NUMBER: N02CO07013-64

Amendment No.: 3

Date of Issuance: May 27, 2010

The above numbered Request for Proposal (RFP) is amended as set forth below. The hour and date specified for receipt of Offerors remains unchanged, **2:00PM local time (Eastern Prevailing Time) on June 4, 2010.**

Offerors MUST acknowledge receipt of the amendment prior to the hour and the date specified in the solicitation or as amended, by separate letter, telegram, or Electronic Mail which includes a reference to the RFP and Amendment number(s). For your convenience, the Proposal Intent Response Form is provided in SECTION J - List of Attachments of this RFP, for this purpose.

FAILURE OF YOUR ACKNOWLEDGMENT TO BE RECEIVED AT THE PLACE DESIGNATED FOR THE RECEIPT OF OFFERORS PRIOR TO THE HOUR AND DATE SPECIFIED MAY RESULT IN REJECTION OF YOUR OFFER.

This Amendment revises the RFP as stated below:

1. Can the awardee contractor for the BCR serve as a TSS through an NCI review and evaluation process?

Response: Yes this is possible. However, the BCR and TSS RFP's are two separate requirements with separate Statements of Work for the respective projects. The proposals submitted in response to the respective RFP's will be evaluated against the evaluation criteria found in Section M for each RFP. Further, your responses for the separate requirements should clearly enumerate all individuals by name, roles detailed and percent effort described.

2. Would the BCR be able to send uniquely identified pre-labeled collection kits to TSSs (as we do with our own collection sites) to more readily integrate the process to our laboratory management and BSI II systems?

Response: This type of system could be useful for our prospective collections and might be able to be integrated at some sites. However, this is not currently in practice nor is it possible for retrospective cases. The offeror must be able to demonstrate the capacity to use a pre-labeled kit and whatever our sites provide already with equal efficiency.

3. As part of our CLIA program, we perform proficiency and competency testing of new employees, as well as annual proficiency and competency testing of all technical staff. For the BCR, would the awardee be responsible for the development of such tests and/or is there a proficiency and competency testing program that exists at the other BCR or within NCI that should be followed?

Response: The offeror, if successful, would be responsible for developing this program but could utilize the NCI COTR for advice/assistance.

4. Is the BCR responsible for TSS audits which occur only after having provided 50 qualified cases to TCGA? Could the audit be performed earlier than after having produced 50 qualified cases to TCGA in the event that there was a problem at the TSS site?

Response: Yes, an audit can be performed at any time in conjunction with the COTR and other relevant program staff. Please note that the BCR would not be responsible for prospective collections by tissue collection network but could be utilized for retrospective sites.

5. The RFP states that the contractor shall use Qiagen AllPrep technology for DNA and RNA isolation. Our "Company X" has a number of in-house protocols using kits with reagents that we manufacture. Would it be acceptable to use our own kits and reagents? We have tested the kits and reagents and found them to be equivalent or better in quality and quantity of DNA/RNA produced in "head-to-head" comparisons with kits from other vendors, including Qiagen. These Company X kits and reagents have been used for in-house projects, Company X grants and Company X contracts, as well used for customer samples for more than 7 years. In addition, these kits and reagents are commercially available to others and have been utilized in many laboratories both in US and abroad.

Response: As long as in a head-to-head comparison they are shown to provide identical or better analytes to our GCCs as well as offer a potential cost benefit, and of course could be shared freely (i.e. with no licensing or other IP costs) with additional BCRs, this could be considered acceptable.

However, since this would require changing protocols might introduce variability in data generated by TCGA centers, it could be that the use of an alternative protocol could not happen, requiring the BCR to adopt the SOPs already in existence in TCGA.

6. Regarding Security and Privacy Requirements on the bottom of p. 37, the RFP states that information systems must implement security controls consistent with a "moderate" level of impact that a breach of security would have on the TCGA program and the sponsoring federal agencies. Where would we be able to obtain specific information on what is a "moderate" level of impact?

Response: The following links should be used to provide additional information.

See Section 3.2 in the following: http://csrc.nist.gov/publications/nistpubs/800-60-rev1/SP800-60_Vol1-Rev1.pdf

http://csrc.nist.gov/drivers/documents/FISMA-final.pdf

7. The RFP it states that case reports forms will be entered online, and on p. 36 it states "A clinical data capture and management system. This system shall capture, manage, and export the patient associated clinical and demographic information. Unless granted a waiver in writing by the COTR, the Contractor shall use the NCI Clinical Data Collection and Management System from Medidata, obtainable under free license, to fulfill the clinical data requirements of this SOW." We were unable to locate the "NCI Clinical Data Collection and Management System" software online, including from Medidata's website. Would it be possible to obtain this software at this time to be able to evaluate it, or would the software be provided to the successful awardee at the beginning of the contract?

Response: All software will be provided to the awardee at time of award as NCI is actively identifying requirements for this system.

8. What would be the procedures for demonstration that our company's current electronic data capture system for case report forms is equivalent or better suited for the contract than the NCI Clinical Data Collection and Management System from Medidata?

Response: The offeror will likely be required to utilize the system that is actively being adopted by the TCGA program and will be in use at the time of award across more than 100 Tissue Source Sites. Note that any change would be implemented only after awards have been made and at that time an offeror could provide alternative approaches. However, no time or resources will be allowed or provided for a "switch" from the software we currently utilize and a new approach and any offeror must be able to integrate into the current system.

9. Under what conditions will archival diagnostic blocks and slides require pathology review?

Response: In most cases the FFPE slides will be reviewed by an External Pathology Committee comprised of expert pathologists from the Disease Working Groups. There are some cancer types, including prostate and thyroid, which may require this review up front. This decision will be made on a tumor-by-tumor basis in coordination with the Program staff and the Disease working group experts.

10. Many cancer sub-types require Immunohistochemical (IHC) staining to confirm diagnosis (e.g. b-cell vs t-cell lymphoma). Will the BCR be responsible for performing IHC and reading these slides to confirm the TSS's diagnosis? If so, will these have to undergo full slide scanning?

Response: To date we do not have any tumor types that require this level of processing that will be processed by the BCR. If a tumor type did enter the pipeline that required this level of processing the BCR would likely have to develop protocols for this level of processing and would be required to complete slide scanning to ensure appropriate inclusion criteria are met.

Alternative to this approach, the BCR could subcontract the work or the NCI may provide a center that would perform the work.

11. Will the BCR be required to verify TSS IHC results for sub-typing, such as ER, PR, and Her2-neu status for breast cancer? If so, will these require full slide scanning?

Response: No.

12. This Contractor has CLIA certification in the subcategory of cytogenetics. In conjunction with new personnel and collaborators/consultants, can the histopathology subcategory of our current CLIA license be obtained after the successful awarding of the contract?

Response: Yes, but we would have to proof of a quality management system at the BCR and documentation and updates on the efforts to become CLIA certified.

13. What is the estimated electronic data storage size requirement to complete this project?

Response: Because genomic and sequencing data are not held at the BCR, but rather only data that is equivalent to excel spreadsheets, the NCI does not believe that the data storage requirements of TCGA are extensive. Electronic storage that is robust enough to support a LIMS and standard business software file storage should be sufficient. The exception to this is the data for diagnostic slides. One could determine the size of a scanned slide and multiply it by the number of slides to be held by the BCR to determine size of data storage required.

14. Will the web interface to allow access to the biospecimens inventory be hosted on a server specified by the contractor or by NCI/TCGA? Where will slide images for EPC review be hosted?

Response: Slide images will be stored in the data coordinating center for TCGA. Yes, the web interface will allow for access to inventory and this will be hosted on a server specified by the NCI/TCGA.

15. Under Section 3.2 of the SOW, bullet three, a protocol is outlined for pathological review which requires specimens for review to be no more than 100 mg and requires front and back sections of each specimen. This could require multiple freezing and thawing of tissue to cut and section, then melt and re-embed to obtain sections of two faces. Has this procedure been used successfully before and proven to be non-detrimental to the RNA and DNA integrity?

Response: Yes. This protocol is in place today with very high success rates for molecular analyte QC. There is no data to support that the cutting of top and bottom sections compromises RNA integrity when performed using the SOPs developed by this program.

16. Would the contractor be advised to have both a general pathologist and also organ/disease specific pathologists available for the successful completion of this contract?

Response: Yes.

However, this does not mean that the BCR has to have an organ/disease specific pathologist on staff for every tumor type studied by TCGA. These specialty pathologists could be temporary contractors utilized while TCGA is working on a tumor type.

17. If the contractor is required to have a whole slide scanning system (such as Aperio), could that be included in the budget for the contract or must that be purchased outside of the government contract funds prior to the commencement of the contract?

Response: Yes, a system like this could be included in the budget for this award.

18. What certifications are required for Biorepository personnel?

Response: PMP for the project manager. Pathologists should be certified by normal accepted means. The PI or other staff leader should be a certified clinical molecular geneticist.

19. In the provided Estimate of Effort table, the estimated number of professional hours anticipated is listed at 202,800 for the base period of 18 months. One FTE for 18 months would account for 3060 hours, so in the Base Period of 18 months, 202,800 hours would require 66.3 Professional FTEs. Likewise for the Option Periods 1 to 3 (if one year each), 135,200 hours would require 65 FTE, and in the Option Period 4, would also require 65 FTE. In the provided Estimate of Effort table, the estimated number of professional hours anticipated to be 65 FTE throughout the life of the contract. Is this estimated number of FTE correct?

Response: Please understand estimate of effort was furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

Yes, the number of FTE is correct.

20. Will the awardees of this contract have access to the "commercial LIMS and subsequent information technology (IT) support system" purchased for the Pilot Project BCR since the various BCRs are expected to communicate closely and share data?

Response: Yes, all offerors will have access to the same systems that are currently in use but will have to let the NCI know what is already in place and what infrastructure would be needed to bring them up to speed. Offerors should include the cost of this in their budget.

21. Does the current BCR utilize the BSI II (Biological Specimen Inventory II) tracking system in addition to the LIMS system?

Response: No.

22. What is the anticipated time of actual arrival of the first samples at the BCR awardees company for processing from the time of the award of the contract?

Response: It will depend on the ramp up time required by the offeror. Samples that are actively being shipped to the current BCRs are continuously ready for shipment.

23. Will SOPs that have been established by the currently active BCR necessarily be required to be followed precisely by the bidder?

Response: Yes unless there is a direct comparison to current SOPs to ensure quality is maintained or exceeded and a subsequent decision by the project to change to another SOP after proper validation has been performed.

24. At what point would the current bidder have the currently active BCR SOPs made available to them?

Response: SOPs will be made available during contract negotiations with offerors in the competitive range.

25. If the current bidder has SOPs that they feel may be superior to the currently active BCR SOPs, would the awardees and the current BCR both be able to perform a "head to head" comparison with the two SOPs to obtain the best SOP for the contract purposes?

Response: Yes, but on a timeframe determined by the NCI and validated according to NCI needs.

26. The use of Whole Genome Amplification (WGA) as a method to "rescue samples originally too small to yield sufficient DNA" can be extremely useful. However, since WGA is no longer genomic DNA but amplified DNA, it necessitates and entirely different handling, quantitation, storage and downstream processing than unamplified genomic DNA. Approximately what percentage of samples tested in various pilot studies required WGA amplification, and therefore required total separation of these samples into a post-PCR environment versus handling, quantitation, storage and downstream processing of genomic unamplified DNA? This applicant firm is very experienced in WGA amplification and handling of post-WGA material, so would it be necessary to utilize the service provider Rubicon for WGA, or is Rubicon specifically contracted to provide an outside QC/QA for WGA for the awardee BCR? The same questions apply for the use of Qiagen to test WGA of DNA for GSC

Response: TCGA is interested in developing the WGA technology "in house" and the offeror can describe their capacity in this area and bring this into their quotation. Note that only about 5-10% of samples are currently rescued with the "rubicon" method but all samples (100%) proceed through Qiagen amplificiation for sequencing.

27. The current applicant does have Clinical Laboratory Improvement Amendments (CLIA) laboratory accreditation, and has ethical, legal and policy SOPs to ensure complete collection and protection of patient information as per HIPAA regulations. However, it is unclear to this investigator in which way the "use of biospecimens and information about them potentially relates to clinical care" necessitating clinical analysis of tissue samples to be at the level of standard of care? Would histopathological data be reinterpreted and returned to the physician in charge of the individuals?

Response: All genotype-phenotype data is made available through a public database therefore clinicians supporting the patients whose samples are donated to TCGA technically will have access to potentially clinically actionable genomic data.
Also, if a pathology review reveals that a mis-diagnosis occurred, the institution providing the sample in question is notified.

28. Should Laser Capture Microdissection (LCR) of specimens be required at a later date, would the acquisition of the equipment, if not owned currently by the awardees, be reimbursed by the government in (perhaps) the same manner that the LIMS system and subsequent information technology (IT) support that required capital investment was handled for the Pilot Project BCR?

Response: Yes, it might be reimbursed by the Government if properly justified, necessary to the project and if funds are available. Request for equipment are reviewed on a case by case bases and not all request are approved.

29. Do the same criteria apply for Molecular Quality Controls for amplification of genomic DNA and WGA DNA apply (production of 500-700 bp, 1000-1500 bp and 2000-2500 bp products)? It is highly unlikely that WGA products will be able to produce amplicons of 2500 bp.

Response: No, the same criteria do not apply for WGA . The offeror can propose molecular quality controls for this material if they have a system in place to test this.

30. This Contractor has established and provided to NCI the multi-locus Sequenom-based SNP analysis to ensure identification sample "mix-up." Our criterion for sample "failure" is a single SNP non-concordance between two putative samples from the same source (this does NOT include assays in which one or both samples do not generate data, in which case the assays are repeated). Are the currently used TCGA criteria allowing a certain percentage of non-concordance between samples putatively from the same individual?

Response: No.

31. In this investigator's experience and that of others, it has been established that RIN values of 6.0 are very frequently acceptable for a large number of molecular biology applications. Should a RIN value fall between 6.0 but less than 7.0, is that RNA sample to be destroyed (the RFP clearly states that RNA with RIN of less than 7.0 should not be sent for characterization, but doesn't state if it should be stored or destroyed)?

Response: The RIN required for this project is 7.0 but samples with RIN <7.0 shall be stored for use in future applications.

32. Would any retroactive labeling of previously collected and stored samples be required to be relabeled using the NCI Global Unique Identifiers (GUID) after the establishment and implementation of the GUID system?

Response: Yes. The offerors will be asked to implement the GUID system within 6 months of contract award on previously processed samples.

33. Are SOPs which titles were provided in Appendix 1 available prior to contract award, or only after the contract has been awarded?

Response: The SOPs will be provided during contract negotiations with eligible offerors that are in competitive range.

34. Are the Illustrative Generic Case Report Forms which titles were provided in Appendix 3 available prior to contract award, or only after the contract has been awarded

Response: These are available upon request.

35. In section J of the RFP, we are asked to complete a form for Targeted/Planned Enrollment Table, PHS-398/2590 (Rev. 6/09).

My understanding is the Tissue Source Sites will be "enrolling" subjects not the BCR.

Response: Correct.

36. Will the organizations submitting a proposal to be a BCR be required to complete the Targeted/ Planned Enrollment Table Enrollment Table, PHS-398/2590 (Rev. 6/09 or will it be Not Applicable (NA)?

Response: The offerors will not need to provide this form.

NOTE: In the questions/responses above, specific organization names have been removed or replaced where possible.

Please be reminded that proposal submission must be received in timely manner prior to the 2:00PM local time (Eastern Prevailing Time) on June 4, 2010, to be considered timely in accordance the instructions outlined in the RFP.

ALL OTHER TERMS AND CONDITIONS OF THIS REQUEST FOR PROPOSAL REMAIN UNCHANGED.