FAQs for the CITN U01 RFA*

1. *The RFA was scheduled to be released in early July and it hasn't appeared. What is happening with this RFA?* We received considerable feedback from the extramural community after the concept was publicized in the April Cancer Letter indicating that the structure of the network as planned (ie., a pre-organized consortia of investigators submitting applications) would not be optimal and likely fragment the immunotherapy community. To accommodate this feedback, it was felt important to delay the RFA in order to modify the organization of the network and various specific aspects of the RFA. Consequently, the release of the RFA is not likely to happen before early Fall of 2009.

2. *What is that planned new structure for the CITN?* Specific details are still subject to appropriate clearances in the process of RFA development. Nonetheless, in the currently planned structure, the RFA will solicit applications for a Central Operations and Biostatistical Office (COBO) only. This Office will be the site of the Principal Investigator of the U01 and applicants for COBO award will not have to be pre-affiliated with any specific clinical trial site. Selection of appropriate Member Clinical Sites will take place post-award. Specific details will be announced later, but this selection process will be competitive and open to all qualified candidates**. Up to 25** member sites are expected to be selected in this manner. Sites will not receive separate awards but will participate in the U01 under subcontractural arrangements and will be compensated based on patient accrual (at a fixed per capita rate).

3. *How will the specific CITN clinical trials be selected?* Concepts for potential clinical trials will be selected by a Steering Committee composed of site leaders from each selected Member site. The selected study concepts will then need to be approved by an independent CTEP-organized review before moving to a protocol writing team.

4. *Won't the trials that are selected be limited to those proposed by the CITN network site leaders primarily?* No, this will be an open system in that any investigator can propose a trial to the Network Steering Committee. Also, any working groups that are formed within the CITN to formulate "best" trials may be composed not only of Steering Committee members but can also include appropriate investigators outside the CITN.

5. *Why is it necessary to have a new Central Operations Office with a PI – isn't there an infrastructure in place that could handle this administrative function?* Since this is an investigator-initiated network functioning under a cooperative agreement, the organization requires leadership, coordination, and the ability to negotiate with industry and the FDA. This requires an academic-based leader working in a supportive institution. However, NCI will make use of the Cancer Trials Support Unit (CTSU) to help this new network manage clinical trials to avoid re-creating an entire clinical trials management structure. *How can the PI be rotated?* Since the U01 will be recompeted after 5 years, there is an opportunity for a new PI

to be installed at that time. This is particularly feasible as the PI's office will not consist of a large number of support staff since the CTSU will manage all aspects of clinical trials administration. *Is there a possibility for a co-PI at a separate institute?* Yes, this option is open (a single co-PI under the NIH multiple PI option to serve as vice-PI in the PI's absence).

6. *Will the Lead Biostatistician to head the CITN Statistics Office in the COBO necessarily come from the CITN Operations Office headquarters?* The Lead Biostatistician isn't required to reside at the same institution as the PI, although he/she will be required to work closely with the CITN Operations Center and the CTSU. Also, COBO applications could come from more than one institution.

7. *Why is the CTSU being used as the data management center for the CITN? Are there not more efficient mechanisms for this infrastructure within academic centers?* The CTSU has been used successfully for efficiently managing Phase 3 and more recently Phase 2 trials run by the NCI cooperative group and by other Phase 2 networks. Based on these earlier efforts, the CTSU has developed efficient systems for managing patient registration, data submission and per patient capitation and specimen collection. Trials and all associated documents will be posted on the CTSU website for easy access to both Member center and ancillary sites. Utilization of the CTSU will avoid the necessity to develop an entirely new infrastructure to support the CITN. NCI has committed funds to the CTSU for management of the initial series of CITN trials.

8. *How many trials are expected to be run by the CITN?* We expect 15-20 Phase I or smaller Phase II trials to be initiated by the Network in the 5 year funding period. *Can randomized Phase II trials be proposed?* Yes

9. *There really aren't sufficient funds allocated in the CITN to do everything that appears to be requested, given the complexity of running optimized immunotherapy clinical trials*. The RFA will state that significant infrastructure to run trials will be managed by the CTSU, including all data management, site activation, regulatory document collection and patient enrollment. Site costs to run the trials as well as specimen collection costs will not be a burden on Member site budgets as these costs will be paid out of CTSU funds and reimbursed on a per capita basis. Regarding laboratory costs for immunomonitoring and biomarker studies that will be charged to the U01, some assays may be more efficiently run by subcontracting to government laboratories, which will reduce U01 expenses. We also expect that the costs of trials will be shared by successful contracting with commercial vendors. Finally, although there are clearly many potential avenues of growth of the field, as a new network, all potential immunotherapy tracks cannot be initiated simultaneously; given the length of time it takes to ramp up the first series of trials and the limitations in obtaining GMP-ready agents for trials. The funding committed in the initial years should be sufficient to determine if this network will be successful in carrying out early phase immunotherapy trials.

10. *Will radioimmunotherapy be an acceptable type of immunotherapy for the CITN, or is this excluded?* Yes, radioimmunotherapy can be included as a systemic therapy.

11. *Are foreign institutions OK?* Canadian but not European institutions would be acceptable as Member Sites, but the PI/Central Operations and Biostatistical Office award will be limited to U.S. institutions.

12. *What about Pediatrics?* Pediatric institutions will be eligible to seek Member Site status, and pediatric clinical trials should not be excluded from consideration.

NEW FAQs as of 9/11/2009:

13. *Will any agents identified as high priority be available from NCI for pre-clinical testing and how do we obtain them?* Yes, we currently have a small stock of IL-15 and IL-12, as well as Ad-CCL21, available for use in pre-clinical studies. You may contact Dr. Steve Creekmore at creekmor@mail.ncifcrf.gov for further information to obtain IL-15 and Ad-CCL21 and Dr. Howard Streicher at CTEP/DCTD (streicherh@mail.nih.gov) to obtain IL-12.

14. *Will there be an opportunity for a multiple PI award?* Yes, a second PI can be named (outside the PI's institution) who would function as a vice-PI, with the PI named as the corresponding PI.

15. *What resources will the PI site need, specifically will it need statisticians, protocol management personnel, database management?* The CTSU will be used for data capture, but data analysis and protocol management will be the responsibility of the Operations Center.

16. *How will reimbursement for correlative studies be handled?* Similar to reimbursement for patient studies, these costs will be reimbursed on a per protocol basis, and a central laboratory will be identified for sample collection and storage; patient specimen collection costs will be included in the capitation reimbursement.

17. *What is the timing of application receipt now that the RFA won't be released until the Fall?* The application receipt date has been planned for the first quarter of 2010; funding is still expected in FY10.

* Note that all of the terms and conditions described in the FAQs are tentative and could be modified in the final RFA