**ET-CTN – Frequently Asked Questions**

**Updated Information is in purple.**

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| **Question** | **Answer** |
| **Multiple PI** |  |
| Can the Multiple Principal Investigator (PI) option be used for applications submitted under this FOA? | Yes, the Multiple PI option can be used for applications submitted under this FOA. This option must be used in compliance with the NIH Multiple PI guidelines <http://grants.nih.gov/grants/multi_pi/>A decision on whether to use the Multiple PI option is left up to the discretion of the applicant. Sites, consortia, and/or organizations determine how to set up the Multiple PI arrangements and how this collaboration will be worked out among all parties involved. |
| For a multiple PDs/PIs application, must all of the AOs be led by a “multiple PD/PI,” which has a specific meaning in the PHS398, or can one or more of the “entities collaborating with the LAO under subcontractual/consortium arrangements (also referred to a Affiliated Organizations, AOs)” be simply a subcontractor, led by a sub-contract PI? | The AO can be led by a subcontract PI. |
| What role does the LAO play in the Multiple PI set up? | The LAO is the site that will receive grant funding and should be viewed as the administrator of the grant. |
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| **Budget** |  |
| The RFA requests that “Detailed Budget for Initial Budget Period and Budget for Entire Proposed Period of Support” include both “a detailed budget (direct costs) for the entire application” and “detailed separate budget information … for the following individual application components….” Does this statement mean that all of the details from the budgets of the individual components must be duplicated on the budget pages for the entire application? Can the budget for the initial budget period list the totals from each of the 6 component budgets? | The budget for the performance sites can be summarized by each budget unit in the budget pages for the entire application. For example:Summary Budget                Scientific Leadership                                Consortium 1 budget                                Consortium 2 Budget                                Consortium 3 budget                Team Science                                Consortium 1 budget                                Consortium 2 Budget                                Consortium 3 budget Etc…..Then submit one budget page that shows what the future year costs will be for each budget unit. |
| Are the subcontractors required to provide the same multiple budget pages by component? | Separate subcontract budget pages are required for each of the 6 listed individual components. However, the subcontract budget pages for the entire application can contain totals from each of the subcontract 6 component budgets. |
| Should costs for IRB approval be included in the budget? | No, costs for IRB approval should not be included in the budget. |
| The same examples “(e.g., blood and urine collection and shipping for PK studies, tumor tissue handling and shipping to the tissue bank, and performance of research imaging studies)” are listed in both the “PK/PD, Biomarker Assays, and Molecular Characterization” component and the “Coordination of Clinical Trials and Associated Activities” component. Is there a distinction between which of these costs are allowed under each of these components or can we chose to include all of these costs under either component? | The PK costs can be listed under either component or listed under each component. It is important to note duplication of the identical costs under both components is not permitted. Indicate in the budget justification that the costs included will be used for both purposes however they are only included in one budget. Administrative supplements and use of other funding mechanisms for PD, Biomarker Assays and Molecular Characterization will be a separate process outside of the funding requested for the ET-CTN grant award. |
| Will the budget proposed for biomarker assays to be “funded separately through administrative supplements” be included within the $850,000 per year budget cap or would this be an allowable exception to the budget cap? | Funding of administrative supplements will be a separate process outside of the funding requested for the ET-CTN grant award. The budget cap of $850,000 total cost per year should not be exceeded. There are no exceptions permitted for exceeding the cap for these UM1 applications.  |
| Should imaging costs be included in the budget? | Funding of administrative supplements for imaging will be a separate process outside of the funding requested for the ET-CTN grant award. |
| What type of imaging will be carried out? | The type of imaging needed will be based on the drug development plan. |
| Was $3,000 total cost the amount the NCI expects to be budgeted per biopsy? | Yes, NCI’s best estimate was $3,000. |
| Should we include shipping and handling in the budget or would NCI be supplying that service? | Shipping and handling should be included in your budget. |
| We plan to have subcontracts on our budget. How will the indirect costs affect the total cost of the application? | The indirect costs would come out of the total cost budget. The maximum allowable total cost for each application is $850,000. |
| There was a recent memo stating that two of the four IDSC annual meetings will be web meetings. Should we only include travel costs for two of the IDSC meetings?  | Applicants should budget for 2 EDD meetings and 2 IDSC meetings annually. As the team development projects are launched, investigators should anticipate 1-2 additional face to face meetings may be requested. Please note that the IDSC will continue to meet four times a year. The LAO PI is required to attend these meetings. Twice a year the IDSC meetings occur in conjunction with the EDD meeting.  |
| Should the budget only include travel costs for 3 representatives going to 2 Early Drug Development meetings and 2 trips to major national meetings for presentation of data? | As the team development projects are launched, investigators should anticipate 1-2 additional face to face meetings may be requested.  |
| Is the submission of an Awaiting Receipt of Application (ARA) letter required for applications submitted under this FOA? | Because this FOA specified a budget cap of more than $500,000 direct costs, submission of an ARA is not required.  |
| Are you envisioning that the career development and mentored training of junior investigators for be approximately 3% of the total budget for salary of the junior investigator?  Or support in other ways (the support of those training the junior investigator; support for travel, etc)? | Approximately 3% of the budget is a very modest amount of money to address training. It is up to the institution how to use this money and how to leverage other institutional resources to further facilitate mentored training for junior investigators. Travel support is one acceptable approach, but would not comprehensively address this issue. Other sites may be contemplating submitting a multi-institutional training grant in experimental therapeutics (separate from this application.) PIs should discuss this with other colleagues to determine the best strategy. |
| We may end up with a budget that exceeds the $850,000 total costs per year. Are we permitted to demonstrate cost-sharing and support from our Cancer Center in the budget? | The proposed budget may NOT exceed $850,000 total costs. You may list other initiatives that support the goals and objects of this grant that are supported out of other cost centers at your institution.  |
| For the initial year when 100 biopsies may not be performed, are we allowed to denote how those funds would be utilized (e.g., go to a pot to fund investigators on the team that otherwise we could not support sufficiently? | While it may be acceptable to assume that you will not reach 100 biopsies per year in the first year, you can provide in the budget a description of how you plan to use the “unused portion” of the biopsy budget to further the translational work and assay development in support of the grant activities. One example may be molecular analysis of paraffin blocks in tumors of interest to evaluate mutations of interest in that disease or from a completed phase 1 study with an expansion cohort. It is recommended that a plan on how to get 100% analysis of tumor tissue molecularly and what you estimate you can do annually be provided in the application.  |
| Can you clarify how under-utilized funds allocated for biopsies may be re-allocated if un-used, e.g. to cover increased accrual (i.e. over the 50 required commitment) on studies that don’t have biopsies? | During the course of conduct for any grant, funds can be reprogrammed to other parts of the project or specific aims. What is required is a statement of the issues, why the reallocation is needed, a rationale and justification for the “new” or revised aim, a revised budget with level of effort, etc. |
| How should we be budgeting for molecular characterization? | We recommend budgeting for 50 molecular characterizations at 2 time points in therapy. The expectation is 100% of patients should be molecularly characterized. What is critical and necessary is obtaining the tissue for analysis. The analysis of the biopsies will be accomplished using a variety of funding mechanisms.  |
| For repeat pharmacodynamic biopsies – should we plan to cover those in some/all of the patients or will such biopsies be covered via supplementary correlative science funding? | When budgeting for biopsies, we suggest sites use the 50 patient minimum. We do not anticipate that all the biopsy funding that is budgeted will be used in the first year of the award, but will ramp up over time. The budget should reflect the reality of the expectation in the FOA that 100% of patients enrolled on study will be molecularly characterized. Thus the budget should reflect the expectations in the FOA.  |
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| **Trial Conduct** |  |
| Can samples be characterized in a non-CLIA laboratory for patients not on treatment? | Yes |
| Does an Investigational Device Exemption have to be submitted for integral biomarker assays? | An IDE may not be needed for all integral biomarker assays. But, if an IDE is required, the NCI Regulatory Affairs Branch in CTEP will provide regulatory assistance to the institution. The NCI will also assist in submissions to the Food and Drug Administration. |
| Are there standard Case Report Forms that must be utilized for studies under the FOA? | Yes. NCI has, through its monitoring and auditing contractor Theradex, 150 standardized Case Report Forms. Included in the 150 Case Report Forms is a standardized Case Report Form for molecular characterization.  |
| What should be included in the application when addressing accrual? | It is important to address outreach and accrual efforts at each site. Of particular interest is the accrual of minorities and those with rare diseases (if applicable).  |
| What criteria are there for selecting an LPO? | The LAO should determine the best qualified investigator to conduct the clinical research project. (Note: Criteria for placement of NCI clinical studies have not changed). The LAO can select a young investigator with a mentor as principal investigator at an LPO. |
| What are the criteria for selection of a submitted project team application (PTA)? | The PTA is reviewed by the NCI program using a competitive review process. Review criteria will include subject matter expertise, existing NCI-funded, peer-reviewed projects, and ability to accrue patients. Sites will be notified if selected for the Drug X Project Team.  |
| How many PTAs will there be for any given drug that will be approved? | All PTAs submitted will be reviewed. The number selected to participate on a project team will be based on merit. |
| What is the role of the LPO? | The LPO is the organization of the principal investigator of the protocol. |
| Is the LPO the leader of the drug development plan, the clinical trial, or both? | The LPO is the leader of the clinical trial. |
| If there is more than one clinical trial, does the LPO lead all of them? | The LPO leads the trial applied for in the PTA.  |
| Is it expected that a separate independent structure be set up to oversee early clinical trials if one already exists in a Cancer Center? | An existing structure for the oversight of early clinical trials in a Cancer Center can be used to oversee early clinical trials.  |
| Is banking of biospecimens being funded under a separate U24?  | Currently, there isn’t a banking U24 in place. The U24 may be recompeted in the future and implemented at a later date. The LAO should make an active plan for biobanking. The LAO may budget for the collection, handling and shipping of specimens until an NCI-funded mechanism for biobanking is in place. |
| What is the minimal or expected annual patient accrual for this program? | Each funded site (UM1) **must accrue a minimum of 50 patients annually.** They may accrue more to accomplish their goals. All budgeted funding should use this number as a basis for calculating a budget. The minimal or expected **capacity and ability to accrue** for the LAO is 50 per year and is 25 per year for the AO.  |
| Can you clarify that the 50 patients per year for the LAO and the 25 patients per year for the AO refer to the institutes’ capacity to accrue? | For the purpose of defining capacity and ability to accrue, documentation is requested in which the LAO documents the ability to accrue 50 patients annually and the AOs demonstrate the ability to accrue 25 patients at their site annually. This information will allow the reviewers to assess how effectively the “site” can accomplish the goals of the FOA by demonstrating ability to accrue.  |
| Is there an expectation that each ET-CTN site open every trial at their site? If so, how are applicants expected to accommodate this cost? How will the PRMS requirements for closure of low accruing studies be modified by the Cancer Center to accommodate this expectation? | The general expectation is each trial will be open to all ET-CTN sites. Under certain NCI approved exceptions, limited institution studies are acceptable. Accrual is reviewed on a monthly/quarterly basis. If accrual is deemed slow, the study will be opened at each ET-CTN site. Discussions with NCI designated Cancer Centers need to be initiated to discuss the issue of low accrual.  |
| Are the agents used for the clinical trials under this FOA those on the list of CTEP agents on the CTEP website? | Yes, the list of CTEP agents is on the website at: [CTEP Agents and Active Agreements](http://ctep.cancer.gov/protocolDevelopment/default.htm#agents_drugs)This list is updated regularly based on IND status. |
| How many members are there on a project team? | It will be determined based on drug development needs. |
| What is the expectation for on treatment biopsies, i.e. how many of the 50 patients should we plan on having a) pre-treatment and on treatment biopsy (i.e. 2 biopsies per patient) or b) pretreatment, on treatment, and at progression (i.e. 3 biopsies per patient).?   Will these “on treatment biopsies” come out of this biopsy funding or be part of translational support supplements? | The number needed/required would be driven by the hypothesis, the protocol requirements, and tissue accessibility. We advise planning for the maximum.  |
| Can Food and Drug Administration (FDA) approved agents, not on the CTEP list, be used for combination studies? | Yes, combination studies with FDA approved drugs are acceptable. The drugs must be licensed for use in the United States by the Food and Drug Administration. |
| Is pharmaceutical company support for part of a clinical study conducted under this FOA acceptable? | There are instances where this may be acceptable. NCI would have to review the agreement with the pharmaceutical company before a determination of acceptability could be made. |
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| **Team Science** |  |
| Does the NCI have a specific preferred approach to team science? | NCI does not have a specific preferred approach to team science. |
| Does the FOA focus on a team science approach through a network process or a team science approach through a consortium process? | Both approaches are acceptable. |
| What characteristics does NCI believe make a successful and effective team? | NCI thinks successful and effective teams have the following characteristics in common:1. Clearly stated common goal/vision
2. Defined roles and responsibilities for each member
3. Defined milestones and timelines that are met
4. Predetermined rules to assign authorship, credit and attribution
5. Defined metrics for success from project initiation to completion
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| Would it be advantageous to submit an application as a consortium with other institutions? | Several approaches can be taken. One approach is not considered more advantageous than any other from NCI’s standpoint.  |
| Would it be advantageous for investigators with very little experience in early phase experimental therapeutic clinical trials to pair with more experienced early phase experimental therapeutic clinical trial investigators? | Yes, it would be advantageous for those who are new investigators to pair with those with experience. If a new investigator pairs with an experienced investigator, they need to provide a communications plan, governance structure, and a clear demonstration that they can meet the goals and objectives of the FOA |
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| **Tables** |  |
| Should the information in the recommended tables in the FOA be provided per institution or per LAO? | The tables are to capture the experience of the applicant. The information should include the LAO, Integrated Components, and AOs. |
| Can the recommended tables be modified? | Yes, the tables can be modified. |
| When instruction and template tables refer to “applicant”, is this the site or the site PI? | “Applicant” refers to the PI at the LAO.  |
| What is the definition of “Cancer Site”? | It is the NCI disease site. |
| Instructions in the templates refer to a 5 year period. When I am reporting “annual” accrual, is this intended to be calendar years or the grant years? | It is intended to be calendar years. |
| Table 1requests information for both the LAO and the AOs. Is this list intended to include the Key Leadership Staffing (a) only for individuals with designated effort on the ET-CTN or (b) the entire organization, including individuals who will interact with and provide resources for the ET-CTN, but will not have a direct role, e.g., the Cancer Center Directors at each of our institutions? | This list is intended for individuals with designated effort on the ET-CTN application. |
| Table 1: How are the key staffing roles defined? | Key staffing roles are defined by the organization. |
| Table 1: Are there any roles that NCI limits to multi-institution applicants? | No |
| Table 1: What is the “Member Designation”? | This refers to the funding mechanism, U01, N01, or Cooperative Group. It can also describe the institutional affiliation if the leadership and other activities are handled by different institutions other than the LAO. |
| Table 2: Can the interpretation of “on-going” clinical trials be any trials accruing subjects or are in follow-up (not yet completed)? | Yes |
| Table 2: What does “Date Trial Closure” mean? |  “Date Trial Closure” refers to the date the trial was completed (follow up (if any) and data analysis completed). What is the most important and/or significant information you want to provide on this table? Finding out how long it took to accrue patients to a trial or how long it takes from accrual to completion – completion meaning data analysis and publication? Reaching the target accrual may go swiftly, but there may be holdups in getting data analyzed and published – be it positive or negative trial results. We suggest adding a column to the table before the “Date Trial Closed” column titled “Date Trial Accrual Closed”. Adding this information would give a clear picture of the accrual success and the time it took to close the trial because of other reasons. It may be helpful to note somewhere on the table, for those trials with long time closure dates, why the trial is not complete (e.g., 10 year follow up,  3 year correlates, etc.). “Date Trial Closed” means time/date for study completion/closure. “Date Accrual Completed” means time/date for accrual completion. |
| Table 2: Does “Total Accrual” mean total accrual in the 5 year period or total accrual for the trial? | It means total accrual in the 5 year period. |
| Table 2: In the instructions it states, “clinical trials for which significant research findings are available”. Should this table only include protocols that have had some kind of publication? | No |
| Table 2: Is this table intended to be a comprehensive list of research activity regardless of publications? | This table is to list research activities the PI(s) feels NCI should be aware of because they are significant. These research activities demonstrate the PI(s)’s and the site(s) ability to effectively conduct early phase clinical trials.  |
| Table 2: Is this a list of all Phase I trials and selected Phase II trials at each of our institutions (LAO and AOs), or only trials approved for credit under the previous U01 mechanism?  | This list is for all trials at each of the LAO and AO (if applicable) institutions. Indicate if the trial is NCI sponsored or supported by other sponsorship. |
| Table 2: Are separate lists requested for the LAO and each of the AOs, or a combined list of the institutions (LAO + AOs) applying as a consortium? As an example, in order to avoid duplication in past applications, we have provided under separate headings Consortium trials (i.e., past U01 trials), SWOG trials (since all institutions are part of SWOG), and institution-specific trials at each institution.  | A combined list of institutions is acceptable. |
| Table 2: For the heading of Column #6, “Primary Endpoint Result-Indication”, what does “indication” refer to? | Indication refers to something that suggests the proper treatment of a particular cancer or a disease. |
| Table 2: What is meant by “Primary Endpoint Result-Indication”? | The primary endpoint for most studies will be dose and schedule determination, as well as toxicity profile and where appropriate, symptom mitigation. It may include biomarkers validation. If the investigation is carried out as a phase 2 clinical trial, the indication would be a disease specific endpoint.  |
| Table 2: For multi-center trials, does “Total Accrual” mean all accrual to the trial or only the LAO, IC and AO sites? | 1. It can be either. Be sure to indicate on the table which accrual you are reporting.
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| For Tables: Are the last 5 calendar years an appropriate timeframe for the last 5 years (i.e., 01JAN2008 – 31DEC2012)? Also – The RFA says last 5 years, but the Guidelines say “past 5-6 years.” Do you have a preference? | The last 5 to 5-1/2 calendar years are acceptable. NCI has no preference. |
| Table 3, Table 4, Table 5: In each case, are these lists and summaries for the entire organization (taking into consideration that only the scientific achievements for Clinical Trials are requested), or only for priorU01-related activities? | These lists and summaries are for the scientific achievements of the entire organization. |
| Table 3: It is not clear what kinds of “Other Scientific Achievements” are to be reported here; can you give some examples? | This table is for a description of what the PD/PI considers a scientific achievement that he/she believes should be mentioned. For example: a prestigious award, a patent, an IND for a particular agent, etc. Anything you consider a significant academic and/or scientific achievement. |
| Table 3: Do the entries in this table have to come from a clinical trial listed in Table 2? | No, this table should not overlap with what is provided in Table 2. |
| Table 4: Can you clarify the difference between Tables 4 and 10? | Table 4 is for PK and PD studies only. Table 10 is for biomarker assay and other correlative laboratory studies performed on patient tissue only.  |
| Table 4: For the entries in Table 4, do they only apply to studies where the analysis was performed “in house”? | Yes, studies by the proposed LAO or AO in the application. |
| Table 4: What does “Year of Request” refer to? | It is the calendar year in which the request for the study was made.  |
| Table 5: Please clarify the distinction between “Phase 2 Tx Studies” and “Phase 2 Combination Tx Studies”. | “Phase 2 Tx Studies” refers to Phase 2 single agent toxicity clinical studies. “Phase 2 Combination Tx Studies” refers to Phase 2 toxicity clinical studies with combination regimes of two or more study agents. |
| Table 5: Should all LAO studies be listed or should all studies conducted by the site PI? | This table should list all high priority studies at all sites involved in the research project (LAO, IC and AO, as applicable). The purpose of this table is to define the capacity and ability of the LAO, IC and AO (as applicable) to conduct early phase experimental therapeutic studies. |
| Table 5: We do not routinely collect screening data from outside institutions on patients who were not registered on the trial. We can obtain the number of patients who signed consent at the LAO (but not the number who were considered for a trial and excluded based on information obtained for routine clinical management not requiring consent). We may be able to obtain accurate information from the AOs. However, it is unlikely that we can obtain accurate information after the fact from other participating sites for multi-site studies which we coordinated. | Provide what you have. We are specifically looking for patients that were screened and were found to be ineligible, for example patients were screened to see if they had a particular biomarker and most were found ineligible because they did not have that particular biomarker. |
| Table 6: What is meant by these two columns – “Accrual to Trial led by Applicant” and “Accrual to Trial NOT lead by Applicant? | “Accrual to Trial Led by Applicant” means clinical trials where the proposed LAO, IC or AO investigators on the application are/were the lead PI on the clinical trial protocol. “Accrual to Trial NOT led by Applicant” means clinical trials where an investigator other than the proposed LAO, IC, or AO on the application was/is the lead PI on the clinical trial protocol and the LAO, IC or AO was a participant (accrued to the trial) on this same protocol. |
| Table 6:Is the information requested only LOI and protocols submitted to CTEP, or to any organization (e.g., NCTN, pharmaceutical companies)? If only to CTEP, then only prior U01, or any mechanism (e.g., SPORE, clinical Program Project)? | The information is requested for LOIs and protocols submitted to any organization. List LOIs and protocols where the LAO or AO was the lead and a participant. It is important to show that the organizations can be both leaders and participants on LOIs. |
| Table 6: Does “Date Submitted” refer to the date the LOI was submitted to the sponsor or the date the LOI was submitted to the institution’s contract office? | It generally refers to the date submitted to the sponsor, but if appropriately labeled you may include the submission date to the institutional contract office which is of less interest to the NCI.  |
| Table 6: Does date approved/disapproved refer to the date the LOI was approved/ disapproved by the sponsor or by the institution’s contract office? | This refers to the NCI decision, but if no studies have been submitted to NCI, if properly labeled, you may use the institutional contract office. |
| Table 6: Does the date “Protocol Submitted” and “Protocol Approved” refer to the date submitted/ approved by the sponsor or the IRB? | In both instances, protocol submission and protocol approval, it is referring to the sponsor (NCI) unless you have no experience working with NCI. If this is the case, it will refer to the sponsor of record and the institutional IRB. |
| Tables 6, 8 and 9: Do these tables refer only to CTEP trials or do we also include investigator-initiated trials supported by industry? | These tables are **not** limited to CTEP trials only. Investigator-initiated trials supported by industry may be included. This is a free and open competition, therefore this is not limited to CTEP or industry sponsored trials. |
| Table 7: Should we provide one table for each LAO and AO? | Yes |
| Table 7: The instructions provided in the Program Guidelines are contradictory on page 95 and page 108.  | The instructions on page 108 are for the FOA application submission only. The instructions on page 95 are for the Annual Progress Report only. Since this is a new competing application submission, the annual progress report instructions do not apply at this time. |
| Table 7: We do not have the ethnicity and race data for industry trials. Can we provide this data for patients enrolled on CTEP trials? | Yes |
| Table 7: Do you want one Inclusion Enrollment Report for each year for all trails of a particular phase (e.g., accrual in 2008 for all Phase I trials combined, accrual in 2009 for all Phase I trials combined, etc. through 1012, and the same for Phase II trials), or do you want total accrual for each trial as requested on the form? (Again, all studies at the institution or only prior U01?) | For the application being submitted under this FOA, one table per clinical trial phase (must be limited to early phase trials only) per year with the total accrual for the year must be submitted in the application. For example, accrual for all phase 1 trials for 2009 should be reported on one table, the total accrual for all phase 1 trials for 2010 should be reported on one table, the accrual for all phase 2 trials for 2009 should be reported on one table, etc.  |
| Table 8: What type of data are you looking for under the column “LOI”? | We are looking for a unique identifier for the Letter of Intent (e.g., LOI number). |
| Table 8, Table 9, Table 10: Do you want data for all studies at the institution or only for the prior U01? | All studies at the institution. |
| Table 8: Does “Operational Efficiency Start Date” refer to a date estimated by the PI for the study to start? | Yes |
| Table 8: Does “Number of Days in Development” refer to the length of time from submission of the LOI until protocol activation or some other time frame? | It refers to the length of time from submission of the LOI to protocol activation, i.e. open to patient enrollment. |
| Table 8: Does “Date of LOI Approval” refer to time of approval by the sponsor or institution? | Either the sponsor or institution. Please make sure you clearly state whose approval you are referring to on the table.  |
| Table 8: Does “Date of First Protocol Submission” refer to submission to the IRB?  | Yes |
| Table 8: Is this table supposed to be only for studies in which the LAO, IC or AO hold the IND? | No, it can be for INDs held by pharmaceutical or federal government sponsors.  |
| Table 8: Does “Number of Days in Development” refer to the length of time from submission of the LOI until protocol activation or some other time frame? | It refers to the date of LOI approval to date protocol is activated. Although we have generally used activation date, it is acceptable to use date first patient enrolled on study. The table column header should be clearly labeled and the analysis consistently applied. |
| Table 8: We do not have LOI dates. Can we use another date, i.e., IRB approval or Protocol Review Committee approval? | Based on the operations of your institution, use a date that is closest to the LOI / concept approval date.  |
| Table 8: The column states “Number of Protocol Revisions”. Does this mean protocol revisions after initial submission to the IRB? | This would be the number of revisions after initial submission to the Protocol Review Committee. The goal is to determine the length of time required for protocol development.  |
| Table 9: What is the difference between the two columns “Estimated Study Closure (i.e. closed to accrual)” and “Anticipate Primary Completion Date”? | *“Estimated Study Closure (i.e. closed to accrual)”* is the estimated date the study is expected to complete the accrual of its planned number of enrollees. “*Anticipate Primary Completion Date”* is the anticipated date that the primary endpoint analysis would be completed. The investigator may add a column that provides the date that accrual was completed. |
| Table 10: What is the purpose of this table? | The purpose of Table 10 is to address patient screening, specimen acquisition, specimen analysis, specimens obtained but inadequate for analysis, results reported out, and screen failure (meaning the integral marker is not identified and thus the patient is ineligible for the study).  |
| Table 10: What information are you looking for under “# of Specimens Requested?”  Is this the number of patients who were asked to agree to a biopsy or biopsies, or is it specimens requested from a tissue bank/etc?  | It is the number of patients who were asked to agree to a biopsy or biopsies. |
|  Table 10: What is the difference between “# of Specimens Completed & Reported” and “# of Specimens Analyzed?” | The number of specimens completed and reported is the number of specimens actually collected and were good enough to bank or use for analysis. The number of specimens analyzed is the number of specimens actually used for some sort of testing, assay, diagnostic, or characterization. |
| Table 11: Are the SOPs requested for the LAO only or for AOs as well? | All that is required is a list with only the name of the SOPs for the LAO and AOs. If the LAO and AO share the same SOP, it only needs to be listed once. **We do not want copies of the SOPs.** |
| Tables 2-10: is the expectation to include data for all applicable clinical trials conducted at our institution or only clinical trials in which the ET-CTN investigators participated? | The primary purpose of the resources tables is to document the PI’s and site(s)’s ability to effectively conduct early phase clinical trials. It should clearly convey the investigators ability to accomplish the goals and objectives of the study. The applicant should use his/her best judgment as to which studies are included.  |
| Can non-CTEP trials (e.g. pharmaceutical trials) be included in any of the tables that fit in the phase ½ category? | Yes, pharmaceutical trials can be included. Pharmaceutical trials should be clearly labeled.  |
| If a study opened in 2006 and accrued until it was closed in 2009, how would the information be reported on the tables? Would the accrual and samples only be reported from 2008-2009? | Accrual information is placed in the table in the year the study was closed or completed. |
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| **RFA/FOA** |  |
| Is this RFA considering new awards or is it only going to re-fund existing awards? | This RFA will fund new awards. |
| Is CTEP open to meetings/calls with Principal Investigators regarding proposed projects after the Letter of Intent (LOI) March 23, 2013 deadline?  | Yes |
| NCI referred to translational components and cancer biology. Are these components included in the RFA? If so, what component will NCI be supplying and what components would an applicant site consider supplying? | Inclusion of cancer biology and translational components are determined by the scope and requirements of the drug development plan. A portion of this work may be covered by administrative supplements.  |
| The FOA is for early phase clinical trials. I am assuming for phase I/2 trials?  | The FOA is for phase 1, early phase 2, phase 0 and pilot early phase clinical trials. |
| What should I do if I still have questions about the RFA/FOA/Guidelines? | If you have further questions, feel free to submit them to the ET-CTN mailbox at **et-ctn@mail.nih.gov** or contact Ms. Caviaunce Johnson **caviaunce.johnson@nih.gov**to arrange an individual conference call with the ET-CTN Program Director. Since the FOA has been released, face to face meetings are not permitted at this time.  |
| Is the specific aims page required as stated in the PHS 398? | Yes, the specific aims page is required. The limit for the aims is one page.  |
| Are the Background pages (3 page limit) stated in the PHS 398 required in the application submission? | The Background information should be included as part of the “Overview of Relevant Capabilities and Past Performance” section in the Research Strategy. Therefore, a separate background section is not required. |
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| **Guidelines** |  |
| When will the ET-CTN Guidelines be posted? | The Guidelines are now posted at: <http://ctep.cancer.gov/investigatorResources/docs/ET-CTN_Program_Guidelines.pdf> |
| Should questions for the Question and Answer Session be mailed in advance of the session? | NCI plans to take questions from all applicants during the Question and Answer Session. Submission of questions in advance of the session is welcome. Submit questions to: ET-CTN@mail.nih.gov.  |
| What specifically will NCI offer in the way of clinical trials management? This will assist in determining our budget for this activity.  | See the Terms and Conditions of Award for Cooperative Agreements for ET-CTN in the ET-CTM Program Guidelines: specifically pages 37-46 (e.g. Medidata Rave, EIRB, etc.) |
| What will the project team application (PTA) consist of? How is this different from an LOI? | A PTA is an application submitted in response to an NCI request to form a project team that will work with NCI to devise a clinical development plan for an investigational agent. The PTA identifies the LPO and project team members, and states capabilities. An LOI is a letter proposing clinical trials utilizing investigational agents held under CTEP IND. An LOI may be in response to a request from CTEP (solicited) or not (unsolicited). Information regarding the submission of LOIs may be found at: <http://ctep.cancer.gov/protocolDevelopment/letter_of_intent.htm>. |
| When will the first Question and Answer session be held? | The first Question and Answer session was **held:** Wednesday, April 3, 2013, 1:00 PM – 3:00 PM Eastern Standard Time (U.S. and Canada EST). **Place:** Virtual Meeting – phone number was available upon registration. Investigators planning to participate pre-registered by e-mail to et-ctn@mail.nih.gov no later than **April 2, 2013**. **In the email, the participants name, affiliation, and contact information was provided.** |
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| What are the responsibilities of the LAO versus the LPO versus the NCI as related to the organization and coordination of clinical trial operations? | See the Terms and Conditions of Award for Cooperative Agreements for ET-CTN in the ET-CTM Program Guidelines: specifically pages 20-56. |
| **Data Management** |  |
| Does the protocol PI have access to all adverse event data in Medidata RAVE? | The PI has access to all adverse event data on their protocol, but not all studies with the drug. |
| Will all adverse event data in Medidata RAVE be available to view in “real time”? | The LPO PI and LPO statistician will have access to the Theradex instance of Medidata RAVE 24 hours a day, 7 days a week. |
| Will LPO sites be required to keep track of registration, screen failures, etc. or will they get weekly print outs by Medidata RAVE? Can we “assume” for now that some of these things will remain static? | Registration will be tracked. If the patient has signed informed consent, then the screen fails will be tracked. If not, the site would need to track this. We suggest that no assumptions be made that these things will remain static.  |
| Using Medidata RAVE, will the LPO PI and LPO statistician have the ability to identify if another site is lagging, in terms of data submission? | By reviewing the data in Medidata RAVE, they should be able to tell if the data submission is timely. Theradex will do QA/QC for timeliness. |
| What data management costs should be included in the budget? | There is a need for sites to enter data into Medidata Rave. The costs to get the required data into Medidata Rave, either manually or by software application, should be included in the budget. These costs must be fully justified in the application. The cost of mailing and handling research-related patient specimens, forms, and materials should be included. The cost of analyzing the data, however, should not be included. |
| Must the Statistician at the LAO oversee statistics provided by the other sites in the LAO? | It is up to the Principal Investigator(s) how the process of oversight of the statistics is conducted. |
| How many times will NCI be auditing sites per year? | Audits will be conducted by the Clinical Trials Monitoring Service (Theradex) at a frequency of 3 times per year consisting of one annual visit and two data audits. It is envisioned that the data audits may be conducted via remote electronic access. Auditing Guidelines for the ET-CTN are available at: at <http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/ET-CTN_Audit_Guidelines.docx>. |
| If a Data and Safety Monitoring Plan exists for an investigator’s institution, must the plan be repeated in the application if submitted in the appendix? | While the Data and Safety Monitoring Plan is not required to be repeated if submitted in the appendix, a short summary of how the Principal Investigator(s) plans to apply the plan to the early phase experimental therapeutic clinical trials proposed in the application is strongly encouraged. This demonstrates the Principal Investigator(s) familiarity and knowledge of the institute’s data and safety monitoring procedures, practices, and requirements. |
| Can we exchange HIPAA training documents to allow open discussion of patients (e.g. tumor board), or will we need to be certified on each institution’s (LAO and AOs) HIPAA training to comply with federal policy? | In order to exchange protected health information with another institution, the research participant must sign a HIPAA Authorization authorizing use and disclosure.  The Authorization should mention the Group and/or Institutions that will receive and/or review protected health information.  For more information please see:<http://www.hhs.gov/ocr/privacy/hipaa/understanding/special/research/index.html> |
| What specific data management and clinical trial registration activities will be managed through a standardized central operational regulatory and administrative support by NCI? | See the Terms and Conditions of Award for Cooperative Agreements for ET-CTN in the ET-CTM Program Guidelines: specifically pages 37-46 (NCI responsibilities are listed in this section). |
| NCI referred to centralized support for safety, auditing, data capturing/monitoring, registration/roster/regulation. Does this mean the LAO application will not have to budget for this or be responsible for this? | NCI anticipates there will be some costs such as filing safety data, capturing and reporting data, rostering patients in Medidata Rave, etc. Expense for the system and auditing will be handling by the NCI.  |
| Will the Central IRB provide approval for the overall research project in addition to approvals for the clinical research studies? | The Central IRB will provide IRB approval for the clinical research studies only. Awardee institutions must get IRB approval for their overall research project from their local IRB. The Central IRB will be the IRB of record for the clinical research studies only. IRB approvals will be tracked in RSS. |
| Can you help me understand how trials will be determined to use OPEN versus IWRS in the future for phase 1 studies? Will all three systems (OPEN, IWRS and RAVE) be used for every trial? | As we move forward, all ET-CTN sites will be rostered in RSS and use OPEN for patient registration. Within OPEN a link to IWRS will be provided to support the LPO with functions relating to slot reservations and cohort management. All ET-CTN protocols will use the Theradex instance of Medidata RAVE. |
| Can you clarify whether each ET-CTN site needs to adopt Medidata RAVE as its clinical trial monitoring system or if the site may continue using its current system but make a plan for linking that system to Medidata RAVE? | All sites/UM1 holders will be required to use Medidata RAVE for reporting for their own studies and required participation on studies initiated in the ET-CTN. Sites will utilize Theradex’s instance of Medidata Rave and Theradex will be responsible for study build, and case report form generation. Reporting will be web based and trial specific.  |
| Are there other informatics tools that need to be compatible with NCI’s platforms? | There are many, please review the CTEP web site for policies and procedures. See: <http://ctep.cancer.gov/investigatorResources/default.htm#data_sharing_links>See the “ET-CTN Informatics and Update Meeting” links.  |
| Now that NCI no longer uses caBIG, is their bioinformatics program defined? | The bioinformatics enterprise is well defined. Patient registration will be facilitated through OPEN and integrated with IWRS for slot reservations and cohort management. PIs will be using the Theradex instance of Medidata RAVE for clinical trials reporting for studies conducted by the ET-CTN. Adverse event reporting will continue to use AdEERS until the CTEP-AERs or the caAERs integration into Medidata Rave is launched.  |
| **Forms** |  |
|  On page 66 of the Guidelines it states under section 2.I.3. Application Submission Procedures: “Submit a signed, typewritten original of the application, including the checklist, and three (3) signed photocopies in one package to the Center for Scientific Review at the address listed below. **The original must be signed by the Project Director/Principal Investigator (PD(s)/PI(s)) and an authorized organizational or institutional official.”** Where do the PD(s)/PI(s) sign? The current Form Page 1 (Rev. 6/09) only has one signature spot for the authorized institutional official. Grants.gov mentioned “revised forms have been approved by OMB and are expected to be implemented in the summer, 2013”- will forms come out in time for UM1 deadline and will it contain spots for PD/PI signature in addition to AO? | NIH Notice Number: NOT-OD-06-054 states:“The signature of the Principal Investigator is no longer required as a part of a submitted application. Instead, a new compliance requirement is now implemented whereby the applicant organization agrees to secure and retain at the organization a written assurance from the Principal Investigator (PI) prior to submitting an application to the PHS.  While this assurance is no longer required as part of the submitted application, it remains a compliance requirement.  Therefore, organizations must retain a unique signature and date for each submitted application.  This assurance must be available to the sponsoring agency or other authorized HHS or Federal officials upon request.  Such an assurance must include at least the following certifications:  (1) that the information submitted within the application is true, complete and accurate to the best of the PI's knowledge; (2) that any false, fictitious, or fraudulent statements or claims may subject the PI to criminal, civil, or administrative penalties; and (3) that the PI agrees to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of the application.  When multiple PIs are proposed in an application, this assurance must be retained for all named PIs. This change is effective with competing applications submitted for submission/receipt dates May 10, 2006 and thereafter.”The requirement for the PI’s signature is no longer needed. It will be removed from the Guidelines in the near future.  |
| Grants.gov mentioned “revised forms have been approved by OMB and are expected to be implemented in the summer, 2013”- will forms come out in time for UM1 deadline? | The forms changing are listed in NIH Notice NOT-OD-12-152 at the following link: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-12-152.html> The PHS 398 form does not appear to be listed in the summary of changes on this notice. In addition, the UM1 application is scheduled to be an electronic submission for applications with an FOA due date on or after January 25, 2014. The ET-CTN FOA application submission date is August 2013. We anticipate the form changes in forms will not impact applications submitted for the ET-CTN FOA. |
| Under Resources, the instructions state, “In addition to standard information, provide in this section documentation of important capabilities and available resources for specific functional components of the ET-CTN LAO.” Is this information requested for the LAO only or the AOs as well? Since this information is requested under “Resources” and not under the section of the Research Plan entitled “*Overview of Relevant Capabilities and Past Performance*,” do the tables include activities of the entire organization or only activities associated with the prior U01. | This information is requested for the LAO and its AOs. This includes activities of the entire organization and is not limited to activities associated with the prior U01. |
| Are investigators restricted to page limitations for each sub-section? | Each sub-section has a specific length that may not be exceeded even if you use fewer pages in another section.  |
| Are there page limitations on the Resources section of the application? | No, the Resources section of the application does not have page limitations.  |
| Is there any specific format for reporting publications? Is the PMCID a requirement for all publications that fall under the public access policy? What about publications that don’t adhere to this policy? Is there a specific format for these? | When citing articles in (a) or (b) below that fall under the Public Access Policy, were authored or co-authored by the applicant and arose from NIH support, provide the NIH Manuscript Submission reference number (e.g., NIHMS97531) or the PubMed Central (PMC) reference number (e.g., PMCID234567) for each article. If the PMCID is not yet available because the Journal submits articles directly to PMC on behalf of their authors, indicate "PMC Journal - In Process." A list of these Journals is posted at: <http://publicaccess.nih.gov/submit_process_journals.htm>.Citations that are not covered by the Public Access Policy, but are publicly available in a free, online format may include URLs or PubMed ID (PMID) numbers along with the full reference (note that copies of these publications are not accepted as appendix material, |
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| **LOI**  |  |
| Is the only indication/description about a proposed submission the “descriptive” title of the Letter of Intent (LOI)?  | Yes, the purpose of the LOI due March 23, 2013 is to inform NCI of the intent to submit a grant in response to this FOA. This information will be used for NCI planning purposes and development of an NCI mailing list for future communications regarding the FOA.  |
| Is there some text or paragraph required in the LOI which describes the project? | The LOI due March 23, 2013 is not intended to be a preliminary description of the proposed project. It is for NCI informational purposes only. |
| How many LOIs will be requested from the project team? | The number is determined by the drug development plan. |
| Will all requested LOIs be approved? | NCI anticipates that the majority of the PTAs selected to participate in the Drug X Project Team will be asked to submit an LOI. The odds are favorable that the LOI will be approved. |
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| **General** |  |
| Are there other responsibilities of the LAO other than the site receiving grant funding and “administrator of the grant”?  | The “duties” outlined in the Program Guidelines (page 28, Section C. “Data Management”, paragraph 1) are most of the duties an LAO would assume. It is up to the applicant to determine the most effective way to do business.  |
| Does the LAO act as the “lead site” during clinical trials and performs data management functions for its AOs? | The “lead site” is not a term used in the FOA. The LAO may be the lead site and do data coordination or define their own functional business model. In general, the site collects and submits data directly and coordinates with the LAO. In a network base system, this would be the most efficient system as we anticipate that most protocols will be open to accrual and treatment network wide.  |
| What is the overall role of the LPO? | The LPO is the idea generator who will write LOIs, PTAs and protocols as well as amendments. The LPO work with and through the LAO and LAO PI. |
| What biomarker assays have already been developed in central labs for use by UM1 projects? | The following is the URL for the publically available assays:  <http://dctd.cancer.gov/ResearchResources/ResearchResources-biomarkers.htm> |
| Is an Awaiting Receipt of Application (ARA) required for this FOA? | No, the ARA is not required for this FOA. This policy applies to unsolicited applications.  Since this is a RFA the policy does not apply.<http://grants.nih.gov/grants/guide/notice-files/not98-030.html> |
| In the Protection of Human Subjects section (page 20/32 of the FOA) it says:  “In addition to standard items indicated in the PHS398 application guide, include in this section SOPs and policies of the proposed ET-CTN related to study monitoring, data monitoring, and conflict of interest issues. Because there is no page limit, do you want the actual SOP?  | Our aim is to receive the Data and Safety Monitoring Plan (DSMP) and the Conflict of interest policy/process. Study monitoring should be part of the DSMP. The DSMP and Conflict of Interest policy and process should be summarized in the human subject section.  In addition, the full Data and Safety Monitoring Plan related to early phase trials and the Conflict of Interest SOP and policy should be included in the Human Subject Section (has no page limit). |