**This transcript is predominately verbatim from the teleconference. It has been edited, and additional comments added, to provide clarity.**

PERCY: This is Percy Ivy speaking. I will be giving a presentation of the questions that were submitted electronically and the answers to those questions. Then we will open it up to a free format which anyone can raise additional questions or ask for clarification. This is a conference call to discuss the Experimental Therapeutics Clinical Trials Network (ET-CTN), RFA-CA-13-006. This is an RFA for the Early Experimental Therapeutics Program. I am going to start by going over some of the most commonly asked questions that we have received since the RFA was released on February 8th of this year.

We will start first with the multiple PI questions. The multiple PI option may be used. It should be used in compliance with the published grant policy guidelines. When we post the FAQs we will give you the url and web link to the published grants policy document that is available on the web. There were a lot of questions about multiple PIs. They follow those guidelines. The sites, the consortia, or the group will have to determine how they are going to set that up and who the PIs will be. They should do that to further their interest and the organization of their group, consortium, or institution. That is a decision that is left up to the applicant.

One of the questions we have gotten is how does the Lead Academic Organization (LAO) play a role in this? The LAO is the site that will get the grant funding, and they should be viewed as the administrator of the grant. It is an administrative function. The group or consortium, if they are multiple PIs, can be organized in any of a variety of ways. There are several models that may be used. It could be a single PI. If you have multiple PIs, you may want to form (for lack of a better description) a triumvirate or something like that if you think you want to guide the scientific and academic direction of your grant. The important thing is that in your application, you describe who the PIs are, how you are going to function as a group within the scope of the network, and how you will work through the coordinating center at the LAO.

 Another question is whether the Affiliated Organization (AO) can be led by a subcontract PI. The answer to that is yes. Are there any additional questions on the multiple PI option?

Okay, we will keep moving. We received a number of questions on the budget. The question is “The RFA requests that a detailed budget for the initial budget period and budget for the 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? We are fortunate to have Shane Woodward from Grants Administration here. If the questions get complicated, I plan to punt them to him. For simplicity’s sake what I can say is that the budgets for the performance sites can be summarized by each budget unit in the budget pages for the entire application. For example, if there is a summary budget for scientific leadership and for each component of the consortium, they submit a budget. For Team Science, each site in the consortium, if there is a consortium, would submit one budget page that shows what future year costs will be for each budget year. Is there any additional clarification that is required by any of the participants?

 PARTICIPANT 1: The overall budget page can just say here’s the cost for this component which is detailed on the next page or on the following pages. Is that correct so we don’t have to relist all of the personnel?

SHANE: No, you do not have to relist all the personnel.

PERCY: Any other questions on this part?

SHANE: In the detailed budgets that follow you can summarize on the first page. However, don’t lump personnel together that are at different institutions. It needs to be a separate budget page for the consortium sites as well as for the parent institution.

PARTICIPANT 1: Just to clarify, so a single institution – you don’t need separate budget pages then?

SHANE: That is correct.

PARTICIPANT 1: You want a budget page for each component within an institution?

SHANE: Yes, we would want a budget page for each component within an institution.

PARTICIPANT 1: And then summarize all of those components for a single institution?

SHANE: Yes

PARTICIPANT 1: For more than one institution, you’ve got multiple pages for the different components at each institution?

SHANE: Correct

PERCY: Okay, moving on. Are the subcontractors required to provide the same multiple budget pages? The answer is yes.

 The next question we got is that the same examples for collection of blood and urine and for PK studies are listed in the PK/PD, Biomarker Assays, and Molecular Characterization. When you characterize your costs, you can list them in the most appropriate place in your application but they should not be duplicated. If you put something in under molecular characterization, you should not duplicate that under PK/PD. It should fit in one place or the other.

PARTICIPANT 1: You don’t care where are long as it’s stipulated what you are listing?

PERCY: That is correct. We are going to move on to questions about trial conduct. One question we received is can samples be characterized in a non-CLIA laboratory for patients not on treatment. The answer is yes. Another question we received was about investigational device exemptions for an integral biomarker- will you get assistance from the NCI? The first thing I want to say is yes there will be regulatory assistance and yes if it is necessary to file an investigational device exemption. The Regulatory Affairs branch at the NCI will work actively with your institution to assure all of that is taken care of. We plan to provide help for individuals. It will be linked directly to an individual study or a specific drug depending on the scope of the drug development plan. We would, at the NCI with the Regulatory Affairs Branch, define with the FDA what we need to do for an investigational agent, specifically as it relates to integral biomarkers which would be used for patient selection of a treatment regimen that will require an investigational device exemption from the FDA.

PARTICIPANT 1: Can I just clarify on this point– If there was an IDE process at an institution that was going to be doing this, they just supply the data to somebody at NCI and NCI puts the package together and will submit it to the FDA? Is that the idea?

PERCY: The NCI will assist in the submission to the FDA.

PARTICIPANT 1: This is a little bit different. You are saying “assist”. Take responsibility for is what I am asking.

PERCY: NCI would have to work with the site because there may be laboratory based information that would need to be included in the IDE. We would be working collaboratively with the site. The NCI, as an entity, could compile that data, write the IDE, then submit it to the FDA.

We are moving on to something called standard case report forms. That comes back to another thing that the NCI is now supporting. Within the context of this RFA, all NCI sponsored trials will use the Theradex instance of Medidata Rave. We will use Medidata Rave as our data reporting system just like we use ACES in the past through Theradex. We will build the protocol for each study in Rave. Once your protocol is approved by CTEP, it will be sent (by approved I mean it is ready to have the protocol built and to get IRB approval) to Theradex to build the protocol. We presume based on the number of standard case report forms that we have developed, we have about 150 standard case report forms in Medidata Rave already for early experimental clinical trials. About 90% of those case report forms can be reused and only about 10% on average (best estimate) would require custom development of the case report form. The plan is to simultaneously build a protocol in Rave and to review and approve it by the IRB of reference which in this case will be the CIRB. The CIRB is in the process of being constituted and we think it will be constituted in June of this year. We will be beta testing that process for implementation in January 2014.

PARTICIPANT 1: The CIRB you are referring to is not the current existing CIRB used for cooperative groups, or is it?

PERCY: It is not the same CIRB. It will be an experimental therapeutics CIRB. Their focus will be the review of phase 1 and some early phase 2 studies. It would include the review of randomized phase 2 studies. The current CIRB that reviews studies for the cooperative groups and by extension what will become the National Clinical Trials Network (NCTN) are not completely maxed out but close to maxed out on the number of studies they can review and approve, the number of amendments, and handling the workload. We felt it necessary to constitute an additional IRB to take on the earlier phase studies. They will share some work and responsibilities. There will be some overlap between the two. This IRB will be constituted with the clinicians and ethicists and individuals that basically would have an expertise that is tilted more towards early phase studies rather than a very late phase studies.

PARTICIPANT 1: Will the IRB be Association for the Accreditation of Human Research Protection Programs (AAHRPP) accredited?

PERCY: It is AAHRPP accredited.

PARTICIPANT 1: Will it be required to state that all institutions will accept that CIRB as the IRB of record for this grant?

PERCY: That is our clear and straightforward preference. It is possible to make exceptions, but my impression is that based on our review of the timelines that it takes IRBs to review and approve studies, they will have to meet a 4 week timeline. You will have to provide documentation that once a protocol is submitted to your local IRB that it can be reviewed and approved within 4 weeks. You are going to have to provide documentation that it can happen. We will be actively tracking it and if that is not happening we will administratively withdraw the study. Our preference is that all sites within the ET-CTN use the CIRB. The reason we constituted it was to assure that we could rapidly implement the NCI sponsored clinical trials and have them ready to go and open at all sites in the network within 4 weeks of CTEP approval.

PARTICIPANT 1: I am assuming that when you submit to your own IRB, because of CTEP now having their own IRB, those costs will not be included in the budget, correct?

PERCY: That is correct.

PARTICIPANT 1: Are the CIRB and the local IRB going to occur sequentially or in parallel?

PERCY: The submissions to the CIRB will occur at the time that the protocol, as a document, is approved by CTEP. If you still have to submit to your local IRB, as soon as you get CTEP approval you should go to your local IRB. Our clear preference is the CIRB be the IRB of record so once that IRB approves that study it will be ready to open in every single site in the ET-CTN. The local IRB must provide documentation that the CIRB is the IRB of record.

PARTICIPANT 2: I switch back from the CIRB to the Case Report Forms (CRF). When you said the 100 or so electronic Case Report Forms (eCRF) you have, does that include CRFs for PK?

PERCY: Yes it does. We’ve developed a PK module. One issue we have had with that module is it only captures individual patient PK values which in context don’t mean a heck of a lot since they have to be analyzed. We would capture the data at the PK reference lab, and we will submit a report on the individual patient to Medidata Rave but at the end of the study the pharmacologist and reference lab will have to develop all the PK analysis and summary reports that are based on all of the patients that are approved on the study to provide an accurate and adequate characterization of the pharmacology of the new agent in the context of the study conducted.

PARTICIPANT 2: As far as Medidata Rave data, once it’s all put in Medidata Rave through Theradex that data would be put out in what format to the PI? What capability and formats will be made available to the PI and the statistician?

PERCY: Medidata Rave is a web based reporting system. All sites, for their individual patient, will enter the data on that patient. All reports from the reference lab will be downloaded into Medidata Rave into a patient specific fashion. Once the PK reference lab, for example, generates a final report on the pharmacology of that specific drug at the end of the study, they do their final analysis and submit a final report for the protocol. My view is since each site is submitting data when they have it and just like the CTMS system the sites are required to submit their data every two weeks, they can submit it at anytime. Therefore the PI of the study will have 100% free access, 24 hours a day, 7 days a week. They can go into the study database at any point in time and they can download specific data sets. My understanding is that you can pull snapshots of all of the data for the patients on the study on Medidata Rave and on an ongoing basis analyze those snapshot views which is basically as of this moment in time - this is the information that has been provided in the system . The PI of the study and the statistician of the study have 100% access to 100% of the data 100% of the time. An individual site that enrolls a patient at their site will have 100% access to all of the data on their patient. They will not have access to all the other patients that are enrolled on the study. That accrues only to the PI and the study statistician. Do you have further questions about that?

PARTICIPANT 2: Yes, that helps. Another clarification: at the end of the study, when I’ve data dumped the data to your statistical group for analysis and publication, presentation, whatever, what format will that be dumped in? Is there going to be multiple options? [Note: The statistician of record for the study will do the analysis not the NCI statistical group.]

PERCY: There are several options. We have been actively, through the last year, been working with Theradex to develop an end of study report. That report would provide all the demographic data. It would provide the compliance data. It would provide the adverse event data. If there was any aggregate analysis data, it would provide it. It would provide charts and tables on that. It would have a brief summary of the background and rationale for the study. There would be a copy of the schema and all of the different data reports. There would be any response data that is provided and documented. We can capture tumor measurements and those kinds of things which we actually have not routinely done, in the context in particular phase 1 studies, but we could capture that. We can generate both response rates and Kaplan-Meier types and waterfall types, and response curves in the context of the study.

We would generate a CRF that the PI would have to fill out, which at the end of the study would document the recommended phase 2 doses, toxicity profile, dose modifications and publications. That report, after less than 30 days of the last patient completing treatment on the study closing, would be generated and sent to the PI of the study.

In addition, the standard way to do this is to generate a SAS data set of all of the data and all of the reports on the study and in that same 30 day window that SAS data set would be sent physically to the study statistician. If, for whatever reason, someone wants the data in a format other than SAS, that can be arranged. The default option will be within 30 days of study closure to send a SAS data set to the PI and study statistician. The other sub report we have developed meets the Food and Drug Administration Amendments Act (FDAAA) requirements because that study will pull more details than what is required under FDAAA. You have to submit to clinicaltrials.gov a summary report that is filed to meet the FDAAA requirements. We will develop a draft report suitable for submission to clinicaltrials.gov and we will send you a copy of that. You can review it, edit it, you can do whatever you want. You can use that for your submission to clinicaltrials.gov to meet the FDAAA requirements for reporting study results in clinicaltrials.gov. We’ve spent the last year developing those reports. We hope that will facilitate the review and analysis of the study and the rapid approach to the publication of any data generated on NCI sponsored trials.

PARTICIPANT 1: So NCI regulatory is not going to submit the report to clinicaltrials.gov?

PERCY: You are absolutely right. They are going to send you a draft. It is your responsibility to submit it. This doesn’t relate to NCI regulatory per se, it is the responsibility of the PI of the study to submit the study report to clinicaltrials.gov under FDAAA. The NCI does not do that. What we have tried to do to make it easier for the sites is to develop a draft report that is annotated in such a way to facilitate the site or PI submitting the end of study report to clinicaltrial.gov but that is not a responsibility that resides with NCI according to the regulations. We are giving you a draft you can work from and sign off on.

PARTICIPANT 1: For reports out from Medidata Rave- I’m sure there are standard reports excluding the dump at the end of the study. For following along on the phase 1 trial, dose escalation, etc. is there going to be any ability to get customization of those reports? In some cases there are correlative pieces of data that need to be fit, such as prior therapy, to look for specific requirements. I am concerned what sort of in between- just, here are the demographics of the people on so far and here is the data at the end of the study. Do we know how that is going to work?

PERCY: The end of study report is compiled contemporaneously. It is updated at the point any one individual enters information. If you look on Tuesday and here’s the adverse event report by dose level and by patient, then on Thursday, you know, if new information has been added, then those tables based on that information will automatically populate and automatically update.

PARTICIPANT 1: Besides the PI and the study statistician, is it possible for the statistician to designate- for either of those individuals to designate somebody else? Just thinking about how we do it now and it actually usually does not go to the study statistician. It goes to another person in biostatistics who then deals with the SAS file and gets the data in a format for the statistician to review.

PERCY: In the context of a specific study, you can designate on the title pages of the protocol who you want it to go to and that individual will be assigned the appropriate permissions in Medidata Rave to look at and/or pull out the snapshot or receive the final SAS database.

Any other questions on this topic? I will clarify a couple of things that get down in the weeds a bit.

What criteria are there in selecting a Lead Protocol Organization (LPO)? The LAO can work with all the investigators within their group to determine who is the most and best qualified investigator to conduct the clinical research project. They can select a young investigator with mentor, or an experienced investigator. Someone can come to the group and say they have this great idea, ”this is a clinical trial I want to do”, but the LAO as the administrator can facilitate the selection of the LPO. The LPO is the institution where the PI for the study resides. That may be at the LAO or AO. It is up to the ET-CTN site to work within their group to select, determine, encourage, or facilitate the selection of the PI at the LPO.

PARTICIPANT 1: On the LPO, our coordination center is our LAO. We have always done things through that coordinating center in going to whichever site within our consortium where the PI resides. The communications to and from everyone on the study goes through that coordinating center. That is important when you are dealing with multiple institutions. I am concerned about who has access to the information.

PERCY: It is up to the applicant to decide how they want to do business. The important thing is that within the scope of your application you provide a communications plan, administrative plan, organizational plan and leadership plan that describes how you as an individual institution or as a consortium plan to do business. That could be weekly meetings, it could be a conference call, or it could be every day conference calls. You will choose to describe for us, in the context of your application, how you as an individual site or as multiple sites plan to conduct your business in general. The important thing is that within the scope of your application you clearly delineate those things.

Project Team Application (PTA)-I will provide an initial example and provide some other clarification. Some of the current U01 holders will be familiar with the process called the pre-solicitation Letter Of Intent. The pre-solicitation Letter of Intent (LOI) is a very abbreviated LOI. The PTA will be quite similar to that. It will be used in a competitive fashion to select the site that will become part of the drug project team. It is described in swim lane 3 in the RFA. You should look at that and review it. What we will be doing with that process is identifying that group or site that appears in a competitive fashion to be the best or most competitive application to participate in refining and finalizing the drug development plan. That is what the PTA will be used for.

 For those of you who are not familiar with the pre-solicitation concept , basically the PTA identifies a small group of individuals who will participate on a drug development project team to define the most appropriate way to develop a new investigational agent that is coming into our program under IND . That group of individuals, which will consist of both clinicians, translational researchers, cancer biologists and project managers, will work together to refine the development plan for that specific agent. They can make a variety of decisions. They could decide we need basically five protocols or subprojects that every patient enrolled on all of those studies need to be molecularly characterized and that only two of the studies need full genome sequencing. They could decide that this is the best biomarker assay that needs to be done in 100% of the patients. They will be making collective decisions on how the best development of the agent should be approached. That will be done in conjunction with the Senior Investigator responsible for the development of the drug at CTEP.

There will be an extensive consultation with the drug company. They will not be doing work duplicative of the ongoing studies that the drug companies are doing. There will be some guidance in the kind of work the NCI anticipates we will be doing in collaborations with their investigators. What the PTA does is it collects the members of that team that will be responsible for finalizing and refining the development plan. That development plan will then be presented by the whole team to the Investigational Drug Steering Committee (IDSC) for review and comment. Any other questions?

I will keep moving. I was asked about the role of the LPO- the organization of the PI on the study. The LPO leads the trial that was used to apply for the PTA. Once the development plan is finalized we will have a list of projects. It is not likely to exceed ten. On average most recently it has been 3-5 projects. Those projects will become protocols. The participants on that team that competed to be part of that project team will be asked to submit an LOI. We anticipate that will markedly decrease the number of LOIs that we receive for a specific drug. What we have been trying to do is to refine the system in a way that a lot of different sites aren’t submitting a multiple number of LOIs with only a 30% or less return rate on their effort to write and submit LOIs that are competitive in the context of developing a specific drug.

PARTICIPANT 2: Can I just clarify, so for example, if you had 5 projects developed from this project team, and you invited applications for people (this group) to submit LOIs. Let’s say out of 5 LOIs intent, 3 of them happened and the other 2 didn’t happen – how are you going to deal with that?

PERCY: Within the project team, we will have had clinical principal investigators submit a PTA. Therefore they have “proposed” a clinical study and we are going make the assumption that after review by program, that’s something in concert with the request of those applications. We would assume that all projects will result in a LOI. It’s possible we may have to go back out and re-identify people but I think based on the presolicitation LOI experience, I don’t think we’re going to be missing projects. If, as the Drug X Project Team reviews all of the proposed studies and what needs to be done, they may make a determination that one of the projects that was selected really shouldn’t go forward and it can be eliminated, in which case, they wouldn’t ask for a LOI for that study or, it could be changed for something else. That would be the guidance that the Drug X Project Team would give both back to the NCI and to the IDSC.

I cannot, because of funding restraints and restrictions, guarantee that 100% of the PTAs that come to participate in the Drug X Project Team and 100% of those LOIs will be approved. I anticipate that they will be approved but if there are funding constraints or other restrictions, it is possible they could be disapproved. One of the decisions we made in taking this approach was that we would be developing the CRADA agreement with the pharmaceutical company in parallel with the definition of the development plan for NCI. If, in the CRADA negotiation process for whatever reason, the company suddenly decided they want to do that study and they don’t want NCI to do it, then that project may need to be eliminated. There are a number of ways in which things could change but my anticipation is that each PTA that is approved and asked to participate in the development team will be asked to submit a LOI. The probability is reasonably high that that LOI would be approved for protocol development.

The next question asks whether all studies would be open at all sites. We have worked towards being flexible. It is possible for a site or a group of sites to propose a limited institution study so that a subset of the ET-CTN sites could initiate the study. That would be acceptable but that specific protocol, if it’s implemented in a limited number of sites, would be monitored for accrual. It would probably be monitored on a monthly basis and have a mass review on a quarterly basis. If for any reason whatsoever accrual was lagging, for example if there were problems with the accrual or there were other issues, it would be opened network wide. I don’t think that is dissimilar from what we are doing currently to comply with the needs of the Operational Efficiency Working Group. Currently, sites get requests for corrective action plans if their accrual is poor; they are asked to add additional sites. In general it’s takes approximately 6 months to get those up and running. Our hope is that by having this kind of global CIRB approval, that if we decide it’s not accruing well and we need to open to all sites within the network, within 24 hours the study will be open to all sites in the network. Does that answer the question about limited institution studies?

 Okay. Another question that we received concerned the NCI designated Cancer Centers. The NCI designated Cancer Centers have a monitoring system for slow accrual on studies conducted or led out of their institution. It is possible that within an institution, the accrual may seem low, poor or slow. I think we will have to work with you and the Cancer Center in particular to discuss how to handle these specific trials. If it’s accruing adequately within the whole network, then it would not make sense at the “lead site” to close it for poor accrual. That is something that we are going to need to discuss further.

We’ve got questions about biobanking. The biospecimens repository RFA, I think, has not been released yet. That is a work in progress. As you plan within this RFA we’re going to have to initially deal with the biobanking of specimens at your institution or a central institution within your consortium. Over the course of the funding period, that U54 for the bio-repository will be released. My understanding is that this entity, the UM1 for early experimental therapeutics, will be part of that competition. We will identify a biorepository that can be used centrally. The most important thing for individual sites to plan is at some point in the future some set of the specimens you receive will need to be sent to a biorepository or biobank. These 2 RFAs are not in sync so one of them is still in process.

PARTICIPANT 1: Can we budget for local banking of specimens therefore?

PERCY: I think you can budget for that and you should simply be aware that at some point in the future that may change. In my opinion, the most critical thing you need to budget for is the specimen collection, handling and shipping, if that becomes necessary at some point. I think there is a level that you already do that in particular for PK specimens- where there’s a reference lab and you have to ship those specimens to the reference lab. The constant costs that I personally see, you need to correct me if I’m wrong, is the collection, shipping and handling of the specimens.

PARTICIPANT 1: When you say collection, my recollection from the RFA is it will be separate money for doing biopsies. We are not expected to take out of our budget to get research biopsies necessary to get specimens – is that true or not true?

PERCY: I think you did not interpret that correctly. Part of the cost within the RFA - this is only an estimate. It was based on an aggregate analysis from a number of contracts the NCI has- that it costs approximately $3,000 using basically image guided biopsies or surgical biopsies to collect tumor specimens for analysis. We would assume, in the context of your grant, that for research studies that $3,000 would be set aside within the grant.

PARTICIPANT 1: Is that $3,000 per patient?

PERCY: Per patient.

PARTICIPANT 1: Per biopsy?

PERCY: Per biopsy.

PARTICIPANT 1: So if there are 2 biopsies on a patient that would $6,000.

PERCY: That is correct.

PARTICIPANT 1: We have to put it into our budget?

PERCY: You should include that in your budget. I should be very, very clear about the way we aggregated this data. It was pretty simple. We looked at the cost schedules for Medicare, Medicaid, and the cost estimates from the institutions that applied to be part of the phase 2 consortia. Based on the estimates that were provided in the context of competing that contract, all we could do is come up with an average cost. We are more than painfully aware that there is a range of costs and it ranges somewhere between $1,500 and $10,000 a biopsy. The range is very broad but there was an aggregate set of intermediate institutional costs at around $3,000.

PARTICIPANT 1: Is that total or direct cost?

PERCY: It’s total cost.

PARTICIPANT 1: One other question in regards to that. If the study is designed such that you need the biopsy to select the patient based on a biomarker and the frequency is 20%, only 1 in 5 patients might even go on the trial. And yet you’ve still incurred that cost.

PERCY: I understand.

PARTICIPANT 1: How is that supposed to be budgeted within the context of this grant?

PERCY: I think that is a challenging question. I think it simply needs to be budgeted within the context of the grant. I don’t think you’re going to find a very satisfactory answer.

 PARTICIPANT 2: That patient won’t undergo 2 biopsies and you take that into consideration, 2 biopsies per patient.

PERCY: Well that is true. One of the ways that we have selected a better description and attempted to ease the pain of this is that over and above the 50 patient minimum we would be able to provide some level accrual credit based on the frequency of expression of the biomarker. I think we’re still in the process of defining these schedules. If we thought that 50% of the patients screened would express the biomarker, making it relatively “easy” to screen patients, then you may get a smaller accrual credit. Whereas if you think it is a 5% marker, you may get a larger accrual credit. We’ve had to make the assumption that some of the patients will come into these studies having already had the biomarker identified from an outside or referral institution, or from the site institution already. There are sites that are routinely screening all their patients when they come to that institution for treatment. They may already have the information upfront. This is basically a very large series of estimates and there is a very large or wide set of variables. There’s a huge standard deviation among institutions as to what it costs to do this. Clearly there are sites that already screen 100% of the patients that come in. That would not require an additional biopsy because that patient would be screened as part of their, for lack of a better description, admission into the institution for treatment.

PARTICIPANT 3: Depending on the number of biopsies actually done per year or per study, would we have flexibility to reallocate that for purposes of increasing accrual?

PERCY: Reallocate what?

PARTICIPANT 3: The biopsy - if we budget to be prepared to do fresh biopsies as opposed to just sending blood or paraffin. Depending on the nature of the studies that come in, I can imagine some won’t need biopsies, some may need a baseline, and some may get a repeat biopsy for any number of purposes. If the actual pattern of accrual per year is such that our estimate for the number of biopsies is either exceeded or over estimated, can we reallocate that money to just simply accrue more patients?

PERCY: Yes. The other thing I should remind all of you is that if these studies are open at all sites, then the cost is technically shared across sites. Not all of the costs the study accrues to the LPO or the LAO. The cost will be spread amongst all sites. If you enroll at a site then the cost, if a site enrolls a patient, for doing the biopsy accrues to that site, not to the LAO. We don’t want to develop a really complex set of business interactions. What you’re assuming, for the purposes of developing your budget, is that you will enroll 50 patients a year at a minimum and that you should plan to do 1 to 2 biopsies on each of those 50 patients. I think that is, in my mind, the simplest way to look at this. If it’s a trial out of your institution, then whenever you put a patient on, you have to do a biopsy. The cost comes from the UM1 cost center. If another site enrolls a patient, then the cost for that accrues to that site or that UM1. You’re not paying for 100% of the biopsies on the trial. Does that make sense to everyone?

PARTICIPANT 1: I understand that from the standpoint of the LPO or something - you’re not paying for all the biopsies that are done in other participating sites. I do think it actually complicates things because it’s going back to the very beginning with the budgeting. There are separate budgets required for each AO. The assumption of the 50 patients will be distributed from the LAO and the AOs. I can tell you, if we have to redo subcontracts because one site does more biopsies than we thought they were going to and another site does less, even though all together we’re getting our 50 patients- that really does cause -it’s not simple. It’s not simple to get the University of California to then go back and renegotiate the subcontract that we’ve already signed. I understand what you’re doing and I’m not sure that there’s an easy solution. I’m just telling you that it doesn’t really simplify the contracts.

PERCY: I don’t disagree with you. As we thought through this, this was the most straightforward solution we could come up with and there are aspects of it that are not highly satisfactory. It really was the best we could do. I would like to remind you all that this is the only RFA that actually received an increase in funding of all the RFAs that were released by the NCI in the last year. In the previous competition cycle, the total cost was around $500,000 and in this competition the total cost for the site is $850,000. So that’s an increase of $350,000. This was really the only RFA that got any increase in funding. I’m sure you’re also painfully aware that whenever the government doesn’t have a budget, when the annual funds are released to the site, part of your total operating budget can be held back until the government, meaning the Congress, has passed a budget for our agency. We’re operating under continuing resolution and there’s a different set of parameters that comes into play. Shane, do you want to add anything about that?

SHANE: Your figures on the increase are correct. In this day and age of funding, we’re not seeing any increases in general on any programs. Most, if not all, are seeing substantial decreases particularly with sequestration.

PARTICIPANT 4: If I understand this correctly, particularly if we’re going to be using biomarkers to qualify patients for eligibility that has to be done in a CLIA certified laboratory, we could be talking about $200,000 to $300,000 just for these biopsies alone. Is that correct?

PERCY: I think that’s a reasonable guess. Anymore questions on this issue?

Okay. One question we received was, can the Food and Drug Administration (FDA) approved agents, that are not on this CTEP list, be used for a combination study? If an agent is licensed for use in the United States through the FDA, then yes it can be used in combination with an investigational agent on this study. We also have, I think, modest to reasonable success in combining 2 IND agents, neither of which is licensed for any indication, and we have investigational-investigational agent combinations. There are about 6 scenarios that play out, but we’ve been, I would say moderately to highly successful in achieving those kinds of combination studies. Then with regard to the pharmaceutical company support, certainly if you develop a CRADA or outside contract with a pharmaceutical company, the most important thing is that the regulatory group here at the NCI needs to review those contracts to assure that there is no conflict with the CRADA agreement that the NCI has in place. But other than that you are certainly welcome to look for, look at and pursue those types of arrangements for additional costs for the study.

I would like to actually bring this up because one of the things we are doing in the context of our CRADA negotiations, and this is another thing that I hope will ease the pain of the cost of the biopsies, is if it is very clear to us, as we discuss the CRADA with the company, that we want to biopsy 100% of the patients on the trial we are proposing, we are asking the company to put funds in the CRADA that we will be able to disperse to the sites to cover the cost of the biopsies or to cover the cost of the analysis. We did not routinely, we sometimes did but not routinely, include that as part of our negotiations but, we are at present including that as part of all of our negotiations with the company. If they think it’s critically important to get a baseline of post-treatment biopsy on every patient on 1, 3 or 5 trials but not on the other ones, then we will negotiate to get the money to facilitate doing that. That is another way that we hope to ease the strain or the burden on the institutions for these cost. We realize that there is, as I mentioned, just a very large variance from institution to institution and even between the U.S. and Canada about what it costs to do these kinds of image-guided surgical biopsies.

PARTICIPANT 2: One question with regards to CRADA and additional funding from drug companies. Have you considered coming up with a way of circumventing distribution of those funds by mechanisms other than a third party contractor?

PERCY: There are a couple of ways we can do that. Basically we can negotiate this through the CRADA. I think there are a couple of ways we can get the money dispersed and we have looked at a couple of ways. The simplest is the CRADA mechanism. All of them require the complexity of the government contractor. We will certainly do the best we can.

I’m going to talk a little bit about team science now. One question is does the NCI have a specific preferred approach? The simple answer is no. At the guidance and direction of our external advisors, the head of the NCI, and our Division Director, we are taking a team science approach. I strongly think that would be the best, most collaborative and most likely to be innovative approach to doing drug development. We hope that it will allow us to take a more prospective approach as we move through the next 5 years of funding in doing drug development at the NCI. The main thing I wanted to say about team science is we feel that team science can be accomplished both through the network, or by a specific team that is assembled by a site.

What characteristics does the NCI believe make a successful team? We think that the team science approach to drug development will lead to more prospective, more efficient, and more creative drug development. We hope that the measure of success in this endeavor will be the rapid development of new treatment strategies and the molecular characterization and biomarker analysis on all patients enrolled in our clinical trials. [From FAQs under Team Science: clearly stated common goal/vision; defined roles, responsibilities, milestones, timelines, and metrics for success; predetermined rules to assign authorship, credit, and attribution]

Another question is whether less experienced investigators would achieve some advantage partnering with more experienced investigators. I think it probably would be advantageous but the more experienced investigators need to define how they want to put together their consortia or their group for their individual institutions. This is a strategic game and you would have to decide what really works best for you. We have been left with the impression that many investigators felt that the NCI had “mandated” that people come in as groups or consortia. There was no such mandate. We attempted to convey that we were open to that but it is not mandated or required. One way we wanted to facilitate that was by the development of a clinical trials network should investigators still want to come in as single institutions. We think it’s terrific that people are collaborating with each other. One of the things that we were charged with is enhancing and facilitating collaboration. If you are doing that I think it’s great but specifically it is not a written as a “requirement” or criteria within the RFA.

 If I don’t have more questions on team science which I welcome and would be delighted to entertain, I’m going move onto the researchers section of the RFA and the ever popular tables. Do I have any other questions on team science?

Okay. The resources section of the document is the only section that does not have any page limitations so I should be clear about that and upfront. The tables, in my mind, are a way for each group, each single institution that comes in, to demonstrate their skill and proficiency with performing early experimental therapeutic clinical trials. In your application, it should reflect the experience of your institution or your group or your consortium. It should include the combined skills of every site that is coming in if multiple sites are coming in. This is a new opportunity meaning it is a Type 1 application. We have changed our mechanism. It is still a cooperative agreement but it is a UM1 rather than a U01. The real goal of these tables is to facilitate our ability to, in particular for new applicants and for previous U01 holders, ascertain how much work you’ve done, how you’ve done it, and how effective you’ve been at implementing clinical trials, accruing to clinical trials, screening patients, those kinds of things. These are not OMB approved tables. They can be modified in any way you would like. It is highly recommended that you submit them. One of the reasons they were developed was to facilitate the review and to have some kind of “standard format” that the reviewers would be able to look at and gain some familiarity with. Although you are welcome to deviate from the tables, my suggestion- it’s not even a strong recommendation-is that within reason you conform to the format of the tables because we are trying to facilitate the NCI-based review process.

There were questions in Table 1 on information about the LAOs and the AOs – is this intended to include the key leadership staffing only for individuals with designated effort? Yes, it is to include leadership with designated effort. It is not necessary to list your Cancer Center Director and lots of others. I don’t want to imply that Cancer Center Directors are extraneous, but we don’t need a lot of other people. We want a list of the key players that are part of the competition for the grant.

In Table 2, is this a list of all phase 1 trials and selected phase 2s or only trials approved for credit under the previous U01? This is a free and open competition. We are accepting new applicants that have not previously had a U01. It needs to include your experience. You can, if you’ve had a U01 in the past, include your U01 experience. Sites coming in *de novo* - they need to very clearly define their experience in experimental therapeutics and why they think they are competitive for this grant. You should list all trials. I think it would be helpful, if you had a U01, to list those studies first. Indicate if you are coming in as a consortium, which sites did what, and how many studies they did because that shows that they are going to be an active and “useful” participant in your consortium. Also, for Table 2, you can combine the list of institutions. Rather than submitting all tables for each institution, you can aggregate all of the information into one set of master tables.

One other question we had was, how “far back” you should go. The simple answer for that is, we wanted your last 5 years of experience in some type of summary fashion. Since there’s a 1 year full cost extension for the current grant, if you want to include 5 or 5 ½ years, that would be fine. You just need to indicate the time period over which you are providing the information.

For tables 3, 4 and 5, in each case, are these lists and summaries for the entire organization? The simple answer is, yes. They should convey the scientific achievements of the organization or organizations that are applying. We have a table for other scientific achievements and sometimes just collecting the data on the clinical trials you did and how you improved doesn’t really give an overriding sense of accomplishment. If individuals at your site or institution received some kind of prestigious award, developed a patent, filed an IND, other things that you consider significant academic or scientific achievements that are not adequately conveyed as you provide information in these tables, then this is a place where you can list those other scientific and academic achievements.

There were questions on table 5. What we were really struggling to get at, and it’s a question that’s actually been raised on this conference call, was information about screening. If you can consent the patient to go on study and for some reason they are a screen failure, we’re trying to capture the expense of screen failures. I am certainly aware of some studies, I can think of one in particular, where we were screening patients for a DLCO. They had about an 80% or 90% screen failure rate. We’re trying to get at that because it’s a cost for the institution to do the screening. We’re trying to develop information that will better inform us on how to approach this as a problem.

With regard to table 6 – is the information requested only LOIs and protocols submitted to CTEP or is it including other things? The simple answer is, it includes any work you have done related to drug development.

There was a question about the inclusion enrollment report, which is a very specific report that the NCI asks for on an annual basis for each study that you conduct. What we want is summary information by year and one large summary table that gives us a sense of the gender, race, and ethnicity of the patients on the experimental therapeutics trials. The information should be, for the Type 5 reports which are annual continuing progress reports, broken out by trial. For the purposes of the submission application, we would like them summarized by year and then summarized over the full period on which you are describing the patients you’ve accrued that would make you competitive for this RFA.

 On tables 8, 9 and 10, we want data for all studies. Once again, what I need to be clear about is this is a free and open competition so it is not a renewal of specific U01s. All sites are recompeting. This is a Type 1 competition. It’s a new funding announcement.

Table 11 - this is another place where we got a lot of questions. We do not want your full Standard Operating Procedures (SOPs) for everything you are doing within your institution. What we want is a list of the SOPs you have. If there is an IRB SOP or specimen collection SOP or whatever kinds of SOPs you have to run at your institution, we just want those SOPs listed in a tabular form. We do not, let me be very clear, we do not want the full SOPs submitted as part of the application.

We got a lot of questions on whether or not non-CTEP trials could be included. The answer to that is yes.

There was a question about studies that span more than 1 year with regard to accrual and what you want to do once the study is completed. You should provide the accrual data for the year in which the study was completed.

 I have a lot of other questions about forms. For most of the answers we’ve referred you back to the Grants Policy or Grants Guidelines, so I am not going to go through those.

I think I’ll open it up now for any questions you have on the phone.

PARTICIPANT 5: Just a couple of things about the forms. For the progress report part where we do the standard inclusion enrollment forms – those should just be for the studies that were in the last progress report period, correct? Studies that were open any time during the last year or, during the current year – is that correct? [Note: This is a new application. The accrual reporting format required for the annual progress report should not be used in the new application submission. Directions for table 7, as described for reporting accrual in the new application, should be followed. ]

PERCY: No, they should cover the 5 year period.

PARTICIPANT 5: Okay, you want individual trials for the full 5 year period.

PERCY: No I want summary, by year, by phase of study, for the period during which you are describing what trials you did.

PERCY: What I’m trying to get at here is how did your institution do in accruing patients, delineating them along gender lines, based on race or ethnicity. You’re filling out the standard table but it is summary information by phase of study. This is so we have a sense if there are any issues. We try to comply with NIH and NCI guidelines related to accruing patients based on race, ethnicity, or even gender. This information should be provided in the context of your last 5 years of work in early experimental therapeutics.

PARTICIPANT 1: I understand that. Because this is a new application, we’re not putting in the standard information as we would do for each non-competitive renewal, the Inclusion Enrollment forms. We’re doing this summary here and I understand we have to do those. In addition to that, do we or do we not have to do the cumulative per study forms that we would normally do in a renewal?

PERCY: This is not for a renewal. You do not do a per study form. We only want high level summary information by phase of study, annually.

PARTICIPANT 6: One question that has not yet been discussed is the imaging question, regarding specifics. You talked about funding biopsies, what type of biopsies, and you also in the RFA specifically discuss imaging and including the cost of imaging. Can you get more specific as to would the imaging costs be included in the budget? What type of imaging you’re necessarily looking for because that’s so drug specific and many times, tumor specific.

PERCY: I think it really depends on how we determine how we want to develop the drug. We will have discussions with the company. If it is very, very clear, it is based on the pre-clinical work the company has done or what kind of studies the company wants. I will take an example that others can probably relate to- we were asked to obtain, this is I guess a different kind of imaging but, cardiac echoes on all patients at baseline enrolled on a specific study. We would negotiate with the company, as part of the CRADA agreement, to defray the costs of those studies because they are study based. They are not part of the standard of care and they are an explicitly defined research cost as opposed to a standard patient care cost. If we needed to do DCE MRI to evaluate response on all of the patients on the study and that was very clear from the get-go; if it was an anti-angiogenic agent and that’s what we thought was the best way to evaluate something, then we would try to negotiate a coverage of at least part of the cost if not all of that cost if it was clear that it was a requirement for the development of the drug. If your institution is doing an investigational imaging study then in all likelihood I think you would need some other kind of funding outside of the scope of the UM1 and outside of the CRADA because that would be a research initiative from your institutional group. I think this would be viewed differently and the cost for that may be viewed differently. We may be able to negotiate getting some help for the cost but in other situations we would not. You would have to get some other source of funding to do a clearly investigational imaging type study. Standard imaging DCE MRI or CAT scans, if it’s required for the study, then we may be able to negotiate that cost. If it is clearly investigational, you may need to seek another resource of funding to do those studies.

PARTICIPANT 6: The bottom line is we do not have to include imaging costs within the context of this budget?

PERCY: That is correct.

PARTICIPANT 7: For table 2, those clinical trials do not need to necessarily have the key personnel or other significant contributors as the PIs? For table 3, the scientific achievements have to be related to clinical trials? Let’s say somebody cloned a gene, you wouldn’t be including that as a key scientific achievement in table 3 – am I correct?

PERCY: I think that is up to you. If you feel that that is a significant clinical achievement of your research group that will have a major impact on the care and treatment of patients, then you may wish to include it.

PARTICIPANT 7: Okay back to table 2 - these do not have to be clinical trials by either key personnel or other significant contributors? It could be someone in your institution that is not listed as a part of this grant?

PERCY: I’m not sure how to answer that. I think what we want is clinical trials related to experimental therapeutics that involve you as a PI or people within your group that are applying for this grant. What you’re trying to do is demonstrate your skill and ability in this area.

PARTICIPANT 7: Got it.

PERCY: I don’t want a list of all trials ever performed at your institution. What I want is, the people that are working within this research area and on this research effort, to demonstrate their skill and expertise in this area.

PARTICIPANT 7: I think you just answered my question, thank you.

PARTICIPANT 4: If we have been the lead institution, are we permitted to include some of the outlying institutions who have contributed patients onto our trials?

PERCY: Yes absolutely.

PARTICIPANT 8: They would have to be part of the current application then?

PERCY: Yes, they would have to be part of the current application.

PARTICIPANT 6: Can I ask you a question related to that? If you are working with other organizations or institutions and they’ve helped you recruit to a trial, it does show collaboration within the context, especially if you were the lead institution of that project. They may not necessarily be going in with you on this grant but I think it’s important that you’ve demonstrated completion of a project in collaboration. You can’t include that data with some asterisk at the bottom of the table?

PERCY: That’s fine.

PARTICIPANT 9: Related to that, if a PI or PIs are migrating from one institution to another, can they count their experiences at the prior institution?

PERCY: That is fine. What I can tell you is, and this becomes a little complicated, sometimes the institution you are leaving will restrict your access to information within that center and you won’t be able to get that information. That is a situation we have run into when people have left one institution and moved to another. Let us just say it was not an amenable departure and the institution can choose to restrict your access to that information. You can provide it, but you may have to annotate it or provide caveats to describe it.

PARTICIPANT 9: Okay.

PERCY: Other questions?

PARTICIPANT 1: In the RFA, under protection of human subjects, it says in addition to the standard human subject items to include the specific SOPs for data, study monitoring, data monitoring, and conflict of interest issues. These should be within the body of the application itself, not as an appendix – is that correct?

PERCY: That is correct. That is an NCI grants requirement.

PARTICIPANT 1: Human subjects are not included in the page limits?

PERCY: That is correct.

PARTICIPANT 1: I just wanted to know if they wanted all 24 pages of the conflict of interest policies at each of the institutions – the answer is yes?

PERCY: You can provide a summary. In my opinion that would be more reasonable, so a summary is acceptable. We can’t have all of that verbiage. I think that would make things easier for the reviewers.

PARTICIPANT 1: Okay.

PERCY: Other questions?

PARTICIPANT 10: On table 5, just in general, what you’re asking is everything on table 2 is supposed to be included in table 5? I mean all the trials that we list are what you want us to include in table 5?

PERCY: Yes.

PARTICIPANT 10: Okay.

PERCY: I have viewed the resource section of this grant, without any page limitations, as the opportunity for you to demonstrate your skills and abilities in the area that makes you competitive for this grant. This is how I view it.

I did get 1 or 2 questions on page limitations. The simple answer is you cannot reallocate your page limitations. If it says this section can be 6 pages, you cannot exceed it. Should you manage to do it in 5 pages, you can’t apply that 1 page you have left over to some other section. The page limitation applies to the section of the grant. That is actually determined by the Division of Extramural Activities (DEA) and grants. You can’t modify those. They only come in specific increments and they were negotiated with DEA for this RFA.

PARTICIPANT 6: Can you repeat the last 2 sentences?

PERCY: The page limitations are negotiated in the context of the RFA with DEA. We sit down and talk with them and say we think our investigators will need this many pages to describe this part. Those page limitations, for whatever arcane reason, come in very specific increments. They cannot be modified, and they can’t be carried over or redistributed in some other part of the grant.

PARTICIPANT 6: Regarding funding for regulatory and data management support personnel at each individual site- you had alluded within the context of the RFA more than once that a lot of the leg work will be done through the NCI mechanism. That has to factor into the equation when we budget out data management and regulatory personnel at each site.

PERCY: We will be centrally managing a lot of the data and data capture in the regulatory work through Medidata RAVE, the CIRB, and through the CTSU for OPEN and Regulatory Support Services (RSS). However, that does not eliminate the need or obviate the need at the site, to have the warm body that enters that information into the system. You have to budget within the context of your application what you need to accomplish that role.

PARTICIPANT 5: Just to go a little deeper into that- that means that for the Medidata RAVE, we’re not responsible for constructing the documents, or the programming that leads to the data capture - that’s all going to be done centrally?

PERCY: That’s correct.

Theradex will receive a copy of the protocol. The protocol will be built in RAVE. They have a set of standard case report forms, and we think that those can be routinely used. Those case report forms cannot be nickel and dimed stuff. They are pretty much set in stone. If you don’t like the order, that’s not a good enough reason to change them. If it’s clear to you that you need to add something, they can be modified. If on a per study basis, you determine that you need an additional or other additional case report forms that have to be customized for that specific study, then we will work with you and Theradex to build those case report forms to facilitate the development of your study.

PARTICIPANT 1: With regards to that, a general issue –registration is going to be run through CTSU using the OPEN system for rostering of all member sites and participants will be done by that mechanism. We won’t have to deal with it as an individual site, depending on which site participates – is that correct?

PERCY: That is my understanding.

PARTICIPANT 5: Okay– who is going to be responsible for data quality and timely submission? Is it going to be the lead site having to have QC people available to change the umpteen sites that are participating in the clinical trial?

PERCY: An overly simplified answer is Theradex will do the first QA/QC. Within the scope of the protocol that they develop there will be a set of flags that are set up that says, within X many days of enrollment, you need to have submitted the following information. If that information has not been submitted on a patient that was enrolled, then you have exceeded the, let’s just pick something random, the 2 week timeframe. You will be contacted by Theradex, meaning the person that enters the patients, to submit that data. We are working out a way to assure that the PI of the study is informed of those communications, because in the final analysis, it’s the PI and the coordinating center for the study that has to take some final responsibility. The data quality and submission will be monitored by Theradex. There are flags and timeframes. If once a month you have to get a CBC on a patient, then a month goes by and they haven’t received it, they’re going to contact the site and say, please submit the CBC results on this patient. They will do that level of data care, monitoring, and cleaning. In the final analysis, it does become the responsibility of the PI. The PI can go into the summary reports for their study. If they look at it and see ten sites that enrolled patients. They only got biopsy information on 3. They can contact Theradex to send out a query to all the other sites to say, you haven’t submitted this information. The responsibility will always reside with the protocol PI but there will be the kind of standard QA/QC that is done by Theradex using Medidata RAVE to make sure that the data submitted makes sense. If there’s something just totally bizarre that didn’t exist then they will send a query and say this thing was submitted incorrectly, please correct or please provide an explanation or whatever. They will do that level of data curration. In the final analysis, it will be the PI that’s responsible.

With regard to auditing, there are things that have changed about auditing. On phase one studies or early clinical trials - they continue to be audited 3 times a year but now, two of the audits will be conducted electronically and only one of them will be a face to face audit for the early phase therapeutic site. Does that answer your question?

PARTICIPANT 6: Yes. Can I ask you another question about table 7 again? The data is only put in there on completed trials? It says completed trials and I would assume that you would want data of all the early therapeutics trials, not necessarily just the completed ones because some of them are ongoing currently over the last year and a half, by the nature of the beast.

PERCY: I hadn’t actually thought of it in that context. What I would say is the following. I would list the completed trials first, then indicate that the other trials are ongoing and indicate the accrual to date or as of a specific time cut off point.

PARTICIPANT 6: What about multi-center clinical trials where there is biomarker analysis? You’re doing signature identification on your patients. If different sites are using different assay technologies and it’s done routinely in those institutions, I’m assuming that because that data’s being used as its CLIA certified it may be okay. We would not have to establish a central assay unless there was something specifically relevant to a special assay?

PERCY: That is correct but the important thing is we are working on developing a reports module. That information will need to be reported to Theradex for that patient and that trial. That information is going to need to be conveyed. We’ve started work on but have not finished those case report forms.

PARTICIPANT 6: Okay, good.

PERCY: Other questions?

PARTICIPANT 6: Because each grant will require a minimum of 50 patients, is it appropriate to set the budget assuming you’re recruiting 50 patients?

PERCY: I think that’s a reasonable assumption.

PARTICIPANT 6: Okay.

PERCY: There are sites that accrue 150 patients a year and obviously we like that. The minimum requirement is 50 patients a year. You’re going to have to figure out how to estimate your budget based on your experience.

Alright, we’re getting down to the last 15 minutes on our time slot.

PARTICIPANT 11: If there are technical or budgetary questions that arise between now and submission of the application is there a hotline or a way that these can be addressed?

PERCY: Well the really good or bad news is that I’m the hotline. As you know we set up an ET-CTN email [ET-CTN@mail.nih.gov]. We will continue to monitor that email address until the grants are due in August of this year. You can email me or you can email the ET-CTN site. With regard to budget questions, I will certainly get all the help and assistance I can from Shane Woodward from the Office of Grants Administration who has been kind enough to attend this conference call with us. We will do our best to answer your queries in a timely fashion. If I cannot accurately answer them myself, I will refer them and get a more definitive answer from an appropriate person.

PARTICIPANT 11: Thank you.

PARTICIPANT 2: Again, sorry to belabor this point but just to be clear- in terms of budgeting we’re talking about 50 patients accrued to trial. Therefore, there’s no budgeting for any screening and screened failures – is that correct?

PERCY: I couldn’t figure out a way to do that. I think it’s important. I think that there have been a lot of discussions internally and externally on how to approach this. In all honesty there was never, in my mind, an adequate consensus. I think you need to budget based on accrued patients who will be participating in the trial. I think we’ll have to continue to work on a way to address frequent screen failures because I hate to say this but I don’t think we really do an adequate job of addressing that issue.

PARTICIPANT 6: Regarding budget as well, I’m assuming that we will be getting no other budget templates specifically related to patient care costs?

PERCY: The budget templates are the standard NIH budget forms.

PARTICIPANT 6: Okay, that’s what I thought. I just wanted to clarify it, thank you.

PERCY: Anybody else with questions? What I can say is the following - we’re keeping the email address open. You are obviously always welcome to contact me. If your site is coming in and you have a lot of specific questions that you feel were not addressed adequately in the scope of this conference call, you’re welcome to call and we will set up a conference call with you to discuss issues related to this RFA. We will provide you with any additional clarification on your submission or answers to questions you have as you review both the RFA and the guidelines. The RFA is a relatively short document. You should peruse it carefully. Please be aware that within that document we have listed explicitly the review criteria that will be sent to the Special Emphasis Panel that will review and evaluate your application. All of that information is in the RFA and it has been expanded in the guidelines. I think it is important to note that the responsibilities of the applicant, the NCI, and both of us together are also extensively outlined both in the RFA and the guidelines. I would use both documents to your advantage. I think it becomes more and more obvious as you look at that- how we have instructed the Special Emphasis Panel to review your application. That will give you some, I hope, very clear sense of what kind of information you need to put in your application.

 I’m going to end the conference call now unless there are other questions. Please don’t hesitate to email me or contact us through our email address if you have an additional need for advice. Thank all of you for attending the call. I appreciate your participation in the process.

PARTICIPANT 6: Thank you very much.

PARTICIPANT 4: Quick question on the budget. It states that there should be a budget for PK, PD, biomarker assays, and molecular characterization research funds inclusive within the budget pages but then it says the biomarker assays will be prioritized and funded separately through administrative supplements. I’m confused.

PERCY: Unfortunately there is more than one answer to that. Let me start with a general statement. Our hope is that part of the biomarker work will be done by the biomarker reference lab here at the NCI. I do not anticipate that 100% of it will be done here. If a reference lab was selected to do biomarkers then it may be possible to obtain some supplemental funding and that would simply be the subject of a discussion.

PARTICIPANT 4: Here’s the question and my grants people will have the same question. If there is some assay we are interested in, I’ll just make up serum VEGF R2. We say we are interested in doing that as a biomarker assay for trials involving angiogenesis inhibitor. We put in a budget for that and assumedly we would budget that per sample or something like that. Is that outside the $850,000 cap?

PERCY: I would think it would be. The way I would approach it conceptually is let’s say we felt that was an essential task for the development of all angiogenesis inhibitors. We would approach the company in the context of our CRADA agreement to negotiate to frame the cost at the reference lab to do that check. It’s going to be, I think, a separate negotiation.

PARTICIPANT 4: Are you going to be sending out some written addendum to the RFA or some FAQs?

PERCY: We are going to be sending out some FAQs. We have a draft and what we are going to have to do is take all of the comments and things we’ve gotten today and make sure they are addressed in the FAQs. Then we will both send them out and we will also post them under the header for the ET-CTN competition on the CTEP website.

[FAQs – go to: <http://ctep.cancer.gov/investigatorResources/foa_et_ctn.htm> and click on the link at the bottom of the web page.]

PARTICIPANT 4: Do you need me to formally send you the question so you that you will be able to formally answer? When we try to submit our grant, our grants people may say oh you’re over $850,000 and there’s a problem or something like that.

PERCY: I think it would be wise for you to go ahead and send it to the ET-CTN email address and I’ll add it to the FAQs. We took minutes for this conference call and we will have everything that’s related to this discussion with 100% assurance that it would get into the FAQs. I think it would be best if you send it to the email address [ET-CTN@mail.nih.gov].

Anything else? Okay I’m signing off. Good bye everybody.

**RECORDING ENDS**