Pre-Application Webinar Transcript for RFA-CA-24-030

Summary Transcript (*) from October 28, 2024, Operations Pre-Application Webinar and Q&A

(*) condensed version of full transcript highlighting the most important information & key points with any Clarifications /Corrections as a companion to the updated Webinar Slides)

Slide 1 - Intro

This is the Pre-Application Webinar for **RFA-CA-24-030: Limited Competition for the NCTN Network Group Operations Centers (U10 Clinical Trial Required)**. The call is being recorded solely for creating a Summary Transcript for the webinar; however, the Webinar slides will be posted on the CTEP website at **https://ctep.cancer.gov/initiativesPrograms/nctn.htm** 2 days after the Webinar.

Slide 2 - Agenda

First, we want to talk just a little bit about eligibility for both organizations and PIs. Then we'll talk about the multi-component application, review criteria, budget, talk about the "Data Management and Sharing Plan", and briefly refer to the Terms of Award. At the end, we will ask for any questions.

Slide 3 – Due Date and Application Basics

As a brief overview of the application, the **application due date is February 24, 2025**. You can submit it earlier if you'd like with earliest submission date being January 24, 2025.

This is a limited competition, with clinical trial required, and only renewals are allowed. It is a U10, which is a multi-project cooperative agreement, so the application is in a modular format with an overall component with 3 cores (or 4 components altogether).

Applicants do not propose specific studies that are fully developed trials for the reviewers to assess per the RFA Review Criteria. This RFA with "clinical trial required" will be submitted with a "delayed onset" record for a series of studies you all will propose during the coming years. The application will be assessed, reviewed, and approved with the Terms of Award from that perspective.

There's now a clinical trial module within all the RFAs which did not exist at the time of the previous U10 recompetition. When they ask you in that clinical trial module if this is delayed start study or delayed onset study, you should indicate this **delayed onset.** Because you will have multiple studies over the next 6-year project period and you do not know/have definitive plans yet on those studies to describe in the application, you will actually only have to make a single entry, and you can title that **"Multiple Delayed Onset Studies"** as the title of the record. There is some other information that goes with that record, but it can be very general. This single study record should go with the "Administrative Core" component. We do not think you'll have to repeat this in each Core, but you can refer back to this "Multiple Delayed Onset Studies" entry, if you do.

The project period is 6 years from March 1, 2026, to February 29, 2032, which is a leap year, so there's 1 extra day. There will be "Just in Time Information", as with any application. Mainly, it

consists of updates to “Other Support” and “Human Subjects Protection Training” for key personnel.

Slide 4 – Eligible Organizations

This has changed slightly from the prior RFA. This is Limited Competition of the US Operations Centers RFA-CA-24-030. **Only current recipients or subrecipients, which have a substantial role in existing NCTN Group Operations Center funded under the current award are eligible to apply. There is a definition of “substantial role” in the RFA-CA-24-030 that must be fulfilled for the application to be accepted for review.**

We are doing this because we know that at least 2 NCTN Group Ops Centers are going to change their grantee institution**. If in fact there are any plans to change any of the other grantee institutions for the Operations Center to something other than the current grantee, please let us know here asap, as we will also have to be in contact with the Office of Grants Administration about that.** But since we knew at least 2 Groups wanted to change the current grantee institution for their Operations Center, the eligibility was written differently this time, but only for the Operations Center RFA. **However, any “new” institution must meet the eligibility criteria listed in the RFA-CA-24-2024 to be eligible under the Limited Competition.**

We also have the same other restrictions as we had before, if you're applying for a Group Operations Center cooperative agreement, the grantee institution cannot be the same institution or organization as that being submitted for associated NCTN SDMC grant for the same project period. Foreign components are allowed, and were allowed last time, and that is mainly for your participation of your ex-US full member sites to participate in trials.

Slide 5 – Program Directors – PD(s) or Principal Investigators – PI(s)

The same restrictions apply for PDs/PIs that we had with the last recompetition, so we will not go through them in detail. If you are a PI or part of a multi-PI group for the Group Operations Center, you cannot be a PI on the Stats/Data Mgt, Canadian, LAPS, IROC, or ITSC cooperative agreements.

Slide 6 – Multi-Component Application

U10 cooperative agreements require a multi-component application, and it is designed around 4 main components. The 1st one is an “Overall component”, and then there are 3 cores: “Administrative Core”, “Clinical Trials Development Core”, and “Member Site Core”. The same page limits as last time are being used and the cores also may or may not have required attachments.

Although there is not something in the RFAs that says you *cannot* submit appendix material, if you read what you can submit under appendix material, it is usually blank forms, blank CRFs, etc. So, there is no reason to do that for a “Delayed Onset” clinical trial application. Otherwise, you are not allowed to provide appendix material unless the RFA explicitly states *specific appendix material* you can include. We did not list anything extra that could be included as appendix material with any component. Requested information for the reviewers is in the attachments for the cores. One other thing though that we did want to point out is NIH has stressed new “Data Management and Sharing Plans” for the application. Those go into the “Other Plans” section of the “Overall Component” of the application.

Slide 7 – Overall Component

We just want to highlight a few things here. Since this is a multi-component/multi-project RFA, so elements are repeated for each component (including the 3 cores). But in the "Overall Component", there are some special items to note.

- Project Narrative should only be in this component. It may be referenced in other parts of the application, but please put the Project Narrative only in the "Overall Component". Other cores actually do not refer to it, so just make sure it is only in the "Overall Component".
- Budget for the "Overall Component" is just the estimated total cost project funding as per the SF424 cover page.
- PHS 398 plan will contain the specific aims and research strategy for the application.
    - *There is a "Resource Sharing Plan." You can read the information for that section, but only put something in that section if you really have something distinct that fits. In the last RFA, the NIH application did not have any specific place to put the Data Sharing plan. Now, there is a specific place for the required "Data Management and Sharing Plan", so you may not have anything that now fits this "Resource Sharing Plan" section.*
- "Data Management and Sharing Plan" for the entire application should be put in "Other Plans" section in the "Overall component". No appendix material really should be provided.
- The "PHS Human Subjects and Clinical Trials Information" form and "PHS Assignment Request" form are in the "Overall component". You can read through the information for these as it is pretty straightforward, but do not fill out the "Human Subjects and Clinical Trials" form in the "Overall component" as that should be in the "Administrative Core".

Slide 8 – All Other Components

The other components consist of the 3 cores, and we will just emphasize a few things.

There is a data safety and monitoring section that is referenced in the "Administrative Core" only. We think that is where the attachment should be for the NCTN Group's "Data Safety and Monitoring Plan". If you cannot find a specific request for it in a specific section of the application, let us know and we have alternative places that could be included. But the only place it is mentioned is in the "Administrative Core" for the NCTN Operations Center RFA (***and if there is no other place to put the DSMB Policy, it should be included following the DSMB Members list in Attachment #3***).

The "Resource Sharing" plan section is probably not applicable, and no appendix materials are really allowed for delayed onset trials since blank CRFs are not informative.

There is also a "PHS Human Subjects and Clinical Trials" information section for the 3 cores. Fill out the delayed onset study form with "Multiple Delayed Onset Studies" in the "Administrative Core" only, and that will complete the requirement for a study entry. That should only need to be in this core, and we think you will not need to fill out the Inclusion Enrollment Report table as everything is delayed onset.

Slide 9 – Summary of Main Component

There are 30 pages for the "Overall Component", which is about the research strategy and the subsections are identical to the last RFA: Significance, Innovation, Approach, and Progress Report. There are no attachments in this section, but there is an "Other Plans" section, and that is where the "Data Management and Sharing Plan" (and "Genomic Data Sharing Plan", if applicable) will go.

The "Administrative Core" is 12 pages, same for the "Clinical Trials Development Core" and the "Member Site Core", and you can see all the attachments listed on the slides.

The "Data Safety and Monitoring (DSMB) Plan", should have its own form within the basic NIH application for the "Administrative Core". But if it does not, there is a required attachment for DSMB members in this core, & you should put your DMSB policy in that attachment with the members list.

Slide 10 – Special Issues

Just to recap some special issues, "Data Management and Sharing Plan "should only be in the "Overall Component".

The "Human Subjects and Clinical Trials" form should only be in the "Administrative Core," with a delayed onset study.

The "Resource Sharing Plan", if you really have something else that fits that section, that is in the "Overall Component".

Special Emphasis Panel reviewers may comment on both the "Data Management and Sharing Plan" and the "Data Safety and Monitoring Board" policy; however, they do not really review & approve them because they are under NIH standard policy. They will have to be reviewed and approved by CTEP before an award can be made, but we will have plenty of time to do that.

Slide 11 – Special Issues Continued

The Project Narrative should only go in the "Overall component".

Key personnel and performance sites should be listed as was done with the previous RFA. Your list of all your trial sites should go in the "Member Site Component".

Slide 12– Accrual

We are requesting accrual exactly the same way as we did for the previous RFA.

We are looking for the unique number of patients when you report accrual. We are not making a distinction there between screening-on-study and intervention accrual. A distinction is made when you have to create your budget for per-case capitation, but not here for reporting.

The accrual should come only from NCTN trials open from March 1, 2019, through August 31, 2024. Also, on the web page, when we post the webinar slides, we'll post an Excel file showing the NCTN trials that were open during that time period (*and we will be updating that list to show the whether the trials were conducted as "IND-Exempt" study, a "CTEP IND" study, or a "Non-CTEP IND" study*).

The accrual should not include studies that were just limited to biospecimen collections or do not have any NCTN funding. When we run the list in our system on NCTN trials, we find this is restricted to just 4 pediatric studies under the Children's Oncology Group (COG) - i.e., 3 older biospecimen collection studies and Project:EveryChild, which isn't a trial/study in the NCTN per se, and any patient who is registered to Project:EveryChild and eventually goes onto an NCI-funded COG clinical trial is counted under the applicable COG treatment trial).

Biospecimens are not considered "accrual" for this application. There are not any attachments reporting on biospecimen collections because the tumor banking grant, overseen by the Cancer Diagnosis Program, funds biobanking not the NCTN Operations Center U10. The only information in this application for biospecimens is related to capitation because we do cover funding for collection by sites under the NCTN Operations Center cooperative agreement. So, biospecimen collections are **only** in the application for inclusion in the **budget** for the "Member Site Core".

Slide13 – Accrual Continued

There is a special attachment for those NCTN Groups who have Canadian members, this is **only** so you can let the reviewers about the accrual from those members **for trials you lead**. For regulatory purposes, if the Canadian Collaborative Clinical Trials Network (CCTG) joins a trial, then Canadian members have to credit CCTG. This attachment lets the reviewers know that those sites were also members of your group as well, and it lets you highlight the collaboration.

For trials that are officially listed on the trial's Title Page as being co-led by 2+ Groups, the reality is only 1 group is the official Lead Group for Operations & Statistics/Data Mgt. If you have studies in this category, you can talk about them in the collaboration area of the application or you can provide an asterisk t at the bottom of the accrual table denoting that is was an official co-led trial.

Slide 14 – Accrual and Timelines

We did take out the accruals for the large Precision Medicine Initiative (PMI) **screening** trials as we did in the previous RFA (i.e., Lung-MAP, ALCHEMIST screening, & Adult MATCH). They're probably not as relevant this time, but we are requiring those accruals to be put in a separate table.

All other trials are in 1 trial table. We did not separate out Pediatric MATCH, since, as of 2019, that study was already changing out of its initial PMI structure into a different format for trial conduct.

For the OEWG timelines, because of the extensive requirements necessary for these types of PMIs, we are asking you **NOT** to include ComboMATCH and myeloMATCH – either the overall screening component or the sub-studies – in the OEWG timelines attachment because of the unique nature and long timelines associated with setting up these initiatives. We did get a question about the iMATCH trial pilot. We initially were not going to exclude it, but given that there are extensive issues to deal with for that effort even if a special IT infrastructure is not being supported by the NCI for the pilot, iMATCH should also be left out of the OEWG timelines. This is a relatively minor change so we will not make an revision to the RFA, but the Webinar slides and this transcript are acknowledgment by CTEP that the iMATCH pilot can be removed from the OEWG timelines table for RFA-CA-24-030.

Slide 15 – Inclusion of Children

The NCTN Program now has network-wide AYA trials that adult groups or the pediatric NCTN Group COG can lead, but if it is an NCTN AYA trial, all groups will be participating. So, per policy, if you are an NCTN adult group and you anticipate leading AYA studies network-wide, you have to address how you will handle that in terms of human subjects protections. That can be done by explaining how you collaborate with COG on those studies to provide protection and oversight of children.

For any question about why you do not include children in your other trials if you are an adult group, you can provide the usual justification for not doing that (i.e., the NCTN has a specific pediatric group dedicated to developing and conducting studies for pediatric patient populations).

Slide 16 – Review Criteria

We wanted to emphasis one aspect of the standard NIH review criteria. Sometimes when people read through the criteria, they will say there is some wording included that sounds like applicants must explicitly propose a new trial for assessment by the reviewers. That is **not** the case.

The review criteria for these applications are related to the research strategy. The studies are **all** multiple delayed onset trials. You do not know what you will be doing exactly over the next project period. However, some of that standard NIH RFA language will refer to a single trial instead of trials and we were not able to change that per se in the RFA. However, there are additional review criteria in the RFA that stress what the intent of this RFA is, which is the research strategy for development & conduct of multiple delayed onset trials over the course of the project period.

We do explain this in conjunction with the Division of Extramural Activities when the Special Emphasis Panel is set up so that there is no confusion for reviewers.

Slide 17 – Criteria and Scoring

The review criteria and the scoring otherwise have not changed. There is an overall impact score for the entire application, and reviewers provide individual criterion scores for the overall application, but not for other components. The other components (i.e., “Administrative Core”, “Clinical Trials Development Core”, and “Member Site Core,”) will receive only an overall adjectival rating.

Slide 18 – Budget Issues

In terms of budget issues, we want to emphasize that the “Overall Component” should just have the estimated total project funding for the entire project period.

Each of the other components do have specific budgets since this is a multi-project application.

Slide 19 – Budget Issues Continued

You want to make sure that your budgets reflect what you think you will do, and you can reference previous experience as well. We do want to point out that there is no funding for the tumor banks, correlative science research per se, or reference laboratories for this application, and we do **not** support costs associated with routine patient care as an expense under this RFA.

Slide 20 – Administrative Core Budget

For the “Administrative Core”, you'll see in that section that there's some minimal effort restrictions for the PIs.

There are also some travel expenses we would like reserved for potential travel to NCTN-related meetings.

Expenses for any alterations or renovations are **not** allowed under this award.

For other expenses, please make sure that you do have appropriate expenses to cover “Data Safety and Monitoring Board (DSMB)” activities and auditing, but also anything else required under the RFA to fulfill the Terms of Award.

Slide 21 – Clinical Development Core Budget

We did want to point out that you can include funding to cover what we call QA/QC functions associated with clinical trials when approved by NCI DCTD/CTEP in protocols (e.g., when a protocol has NCI approval for central pathology review because NCI approved it as something that was required because it was an integral part of the trial or part of an approved integrated component).

Other activities that can be considered allowable costs under this cooperative agreement include central review of NCI DCTD/CTEP approved integral or integrated radiographic images, study team determination of dosing, administration of agents, and review of protocol-specified surgical procedures, etc. You can include cost for staff/investigators doing these types of activities under the grant when these QA/QC functions are approved for specific trial(s) by NCI DCTD/CTEP.

However, any budget for scientific services related to development of innovations in advanced imaging or radiotherapy are only allowed for the 2 groups which were identified at the beginning of the NCTN to have special considerations in these areas. ECOG-ACRIN is designated to conduct primary advanced imaging studies and NRG has some additional funding for radiotherapy treatment innovation. Those have existed since the beginning of the NCTN and the activities are specified in the RFA and were explicitly funded in the previous and current funding periods.

Slide 22 – Member Site Core Budget

Proposed per-case capitation by type of study for members sites are provided in the RFA.

Regarding the budget increase that was presented for the NCTN Program overall to the NCI Board of Scientific Advisors and recommended by the BSA, part of that was to go to the cooperative agreements and part to the contracts that support the NCTN infrastructure for all the NCTN Program components. We do not know what funding will be available in FY2026 for any awards under the NCTN Program at this time. Although the RFA lists per-case capitation increases, we want to emphasize that we do not know what funding levels will be available for awards as funding decisions are not made until the time of award. This per-case capitation listed in the RFA should be considered a ceiling & you can developing your budgets with the information presented in the RFA.

We also want to emphasize that although the NCTN Program sometimes covers the cost of collection of radiographic images at sites for an NCI DCTD/CTEP approved integral trial element

(and occasionally for an integrated study element), no funding is available for optional collections of imaging under the Program (unlike biospecimen collections). So, cost of approved NCI DCTD/CTEP integral/integrated image collection is **not** included here because it usually ends up being a relatively small cost over the entire project period.

Slide 23 – Special Budget Issues

There are also a couple of other special budget issues in the RFA. We do not have LAPS (Lead Academic Participating Sites) for the pediatric sites. Instead, the pediatric group (COG) provides that aspect for its sites differently. This is explicitly referenced in the RFA for the pediatric group However, this funding is separate and distinct from regular capitation and funding for this is restricted at a certain level per the award made to the pediatric group.

Additional capitation for unreimbursed imaging is provided to ECOG-ACRIN when it conducts a primary advanced imaging study. This is beyond the base capitation amount that is in all your budgets and ECOG-ACRIN has separate funding to cover unreimbursed imaging to all sites. This per-case funding is then provided out of ECOG-ACRIN's capitation budget for this category to all NCTN sites, no matter which group the site credits with accrual to the primary imaging study.

Slide 24 – Data Management and Sharing Plan (DMS) [and Genomic Data Sharing Plan (GDS), if applicable]

A "Data Management and Sharing Plan" and a "Genomic Data Sharing Plan (GDS)", if applicable, have to be provided with the application. There are requirements outlined in the NIH grants policy statement for them. Our current data sharing plan does not really address all those elements.

There also is a template for the "Data Management and Sharing Plan (DMS)" and/or "Genomic Data Sharing (GDS)" available at **DMS-Plan-blank-format-page.docx .** We will also be providing a prototype of an acceptable data management and sharing plan when we post the transcript. It will be a prototype similar to what we have done in the past but updated to meet NIH requirements and you may need to provide justification on why you cannot share certain elements. You could also add to this prototype or clarify things, but in the end, even though reviewers may comment on the DMS and/or GDS plans, CTEP program staff will have to review and approve the plans prior to award. We are providing a prototype to show you something that we could approve, and it will not go very far outside the boundaries of what you are already doing right now.

Slide 25 – Terms of Award

The last slide is just to say that the NIH Grants Policy Statement is included in the standard Terms of Award along with specific Cooperative Agreement Terms and Conditions of Award, and those are categorized in the RFA. So, we'll stop here and open it up if there are any questions.

Questions and Answers

Note: questions unrelated to the RFA were not included.

Q: Should the ComboMATCH screening protocol also be included with the PMI accrual and separated from the regular accrual?

A: No, we are not excluding ComboMATCH or MyeloMATCH from the regular accrual. The reason for that is they started recently, so there is not a lot of accrual to those initiatives or to the iMATCH pilot yet, so we did not think it was necessary to separate them out. We only separated out the older ones because we had done that previously, even though they're winding down. The big thing that we wanted to exclude with respect to the new PMIs (i.e., ComboMATCH, MyeloMATCH, and the iMATCH pilot) were the OEWG timelines because those are quite different than anything due to extensive requirements and longer timelines required to build up the PMI infrastructure.

Q: Should A151804, the Immune-Related AEs study, be excluded from the accrual attachments?

A: No, we are not excluding this study because it does have data collection for clinical information in addition to biospecimens and it had moonshot funding as well. The ones we referred to removing are very old studies that were supposed to be phased out and only had biospecimen funding or no NCTN funding at all, while the irAE study has funding for clinical data as well as the biospecimens.

Q: Is the Canadian members accrual table optional or required?

A: The table is optional, but we think attaching something may be required so you can put an attachment there that just says this was an optional table per program and you are not providing it, if that is what you want to do that. When we set up attachments, NIH looks for the attachments, & if one is missing, this may hold up/invalidate the application. You do not want that to happen. This is also something that was requested for prior project periods, so we included it this time as well.

Q: If we are just submitting a delayed onset study record, do we have to include the justification about the inclusion of children? Where should we put the DSMB information?

A: The inclusion of children information may not be required anywhere since you will be entering delayed onset studies in the Human Subjects and Clinical Trials Information form, and very little information is required in this situation, but we wanted to make that available just in case you are asked in the application to say something regarding this issue. The delayed onset study record might also mean there is no clear place to put the DSMB policy information, so just put that as part of the attachment with the DSMB members list in the "Administrative Core" if you are not prompted in the online application to put it anywhere else. DCTD/CTEP can tell the Division of Extramural Activities (DEA) where it is for DEA to guide Special Emphasis Panel members as to where to find it. As previously stated, the DSMB it something the reviewers look at and can comment on, but it really has no bearing on the overall impact score, as reviewers know that it has to follow certain NIH and NCI guidelines, and the NCI program for the RFA will have to review and approve it prior to award.

Q: Should accrual to the NCICOVID study, NCCAPS, be counted?

A: Yes, accrual to that study counts and it will be included in the Excel file List of NCTN trials.

Q: If a patient is enrolled to the ComboMATCH or MyeloMATCH screening study and then enrolls to one of the treatment studies, should they be counted in both places?

A: Yes, because they are separate trials with separate trial numbers. ComboMATCH screening is EAY191, and then the treatment trial is EAY191-XXX. For the big PMIs where the screening is separated out as a separate trial, the unique patients enrolled per trial would include the screening trial accrual and the treatment trial accrual separately. For all other NCTN trials, if the trial has an

embedded screening component within the study (regular trial that is not one of those big PMIs), we are only request the unique number of accruals be presented to reviewers. The reason we did not split that out for the new PMIs was simply because they are so new during the reporting time period that it was not worth the effort to make a special request for that.

Additional Topic: International Members.

Whenever we have a new award, we have to request State Department clearance for all ex-US components for the new project period. For the NCTN Operations Centers, that's mostly ex-US member sites that are full members of your group or are non-member collaborators participating in your studies.

The NCI Office of Grants Administration allows us a grace period for that process to take place for the new project period starting when we know an award will be made. Last time, I think it was almost a 6 to 9-month period before we could get everybody through. So as long as the ex-US member site or non-member collaborator was in good standing at the time of the grant.

Because of that, we will not take in new ex-US full members during this last period (current grant year) as of now unless there is something exceptional going on or it had been pre-planned and explicitly approved by the NCTN Program Director. This is particularly true for new sites in new countries. Any new ex-US full members requests will be delayed until such time as we can get through this period to the new award and that may also include new non-member collaborators depending on the situation. Obviously, if there's something exceptional going on, we always try to do the best we can, but it's a huge amount of work. And technically, an award is not supposed to be made until all those foreign components (which will include all ex-US full member sites and non-member collaborators) are through the State Department clearance process, and it is a huge amount of work to get through that clearance process for all the NCTN groups at the same time. However, there will be a cutoff timepoint at which if the site is not cleared, the site will not be able to enroll patients if it does not have State Department approval for new project period.