Stimulating Peripheral Activity to Relieve Conditions (SPARC)

Informational Webinar

March 24, 2016

Transcript

DR. TAGLE: So good afternoon, everyone. This is the informational webinar on the NIH Common Fund on Stimulating Peripheral Activity to Relieve Conditions, or SPARC for short. I'm Dan Tagle. I'm with NCATS, and I will be briefly giving an overview of the NIH Common Fund and the activities that led to SPARC. And this will be followed by presentations from Dr. Jill Carrington on the biology aspects of SPARC and then on the generation of new technologies from Dr. Grace Peng. I will be speaking on new market indications, and Dr. Vinay Pai will talk on data coordination. Kristina Faulk is also on the line to answer any questions that might be represented already on our FAQ website.

So, Grace can you—next slide? Thank you.

[SLIDE]

Yes, so this is just a broad overview of the current activities being supported by the NIH Common Fund, so just about almost two dozen projects that are ongoing that can fall broadly into four different categories. One would be, as indicated in the green, New Types of Clinical Partnerships, and then you have the Transformative Workforce indicated in blue, and then New Paradigms in Science indicated in red, and where SPARC falls with a number of different activities being supported by the NIH Common Fund would be under Data Tools and Method Generation.

The next slide, Grace.

[SLIDE]

Yes, so what does it take for a program to be supported by the NIH Common Fund? Well, number one is that it has to address a very important challenge or obstacle in the medical scientific community. And it's actually to take advantage of emerging scientific opportunities. The program also has to be very catalytic such that the NIH Common Fund strategic investment in this area will have a wide impact in the field and would generally be achievable within five to ten years.

All the programs are essentially goal driven; that is, they have milestones or benchmarks, which are typically yearly milestones by which each of the funded projects will be assessed, as well as the overall program is also milestone driven.

NIH Common Fund programs are typically crosscutting; that is, they are of federal interest and seek to serve the missions of the 28 Institutes and Centers within the NIH. And because the programs are inherently very multidisciplinary, it requires a high level of coordination not only within the

consortium—or within awarded activities that are funded. That is, each of the awards are expected to coordinate with one another, almost like in a consortium-like activity, but there is also coordination within the awardees and NIH staff.

And then hit the button again, Grace.

The SPARC program in some ways is not necessary unique in that aspect; that is, SPARC will require a high level of coordination, and in some ways activities funded by SPARC are true, but in addition, SPARC, because of the way the field is fastly moving and the need to engage with nontraditional partners, it requires also a new type of funding mechanism, which you will hear about in the next few slides. And so that would be providing a high level of flexibility within NIH to be able manage scientifically the SPARC program.

So, next slide.

[SLIDE]

So, this just in some ways shows the background activities that took place within the NIH in terms of planning for SPARC. As you can see, there was an external input that was obtained through the NIH-Industry Bioelectronics Medicines Summit that was held in 2013, and that was essentially to look at what possible projects might be supported and identifying who the potential partners are and the stakeholders are in the field. Not soon after that, an NIH working group was assembled within NIH that is made up of representatives of a number of Institutes and Centers at the NIH, as indicated in the slide. And we have also continued to engage other federal agencies, including the FDA, DARPA, and in the private sector in terms of large pharmaceutical companies as well as the device manufacturers.

The NIH project team has also done an extensive portfolio analysis to identify what is ongoing research that is currently being funded, what areas need further funding or encouragement to spur the field forward, and part of that exercise was the issuance of RFIs, Requests for Information, for each of the aspects that we have identified as needing key investment by the NIH Common Fund, and that would be in biology, in generation of technologies, in new market indications, and in the data management.

The next slide, Grace.

[SLIDE]

MS. FAULK: Hi Dan; this is Kristina. I'd like to interrupt just briefly to remind people on the phone to mute themselves because we are recording this and will post it on our website. And all of the typing and background notification pings can be very disruptive. So if you could please mute yourselves, that would be really appreciated. Thank you.

DR. TAGLE: Thank you, Kristina.

And so after all these activities, there was a planning workshop that was held at the NIH in February of last year where experts from the various disciplines were in attendance, and essentially

looking at opportunities in biology and technology and data coordination in terms of what needs to be developed, what are the things that need to be focused on within the program, what is feasible and trackable within the program, and what can we hope to achieve in five to ten years timeline. And these are just shown in this slide.

Again, this slide set will also be made available as part of the recorded transcript of this meeting, so that will be something that you can also go back to.

The next slide, Grace, please.

[SLIDE]

And so the NIH Common Fund then decided to invest approximately $200 million to the SPARC program over the next seven years. And what we really hope to achieve with this investment would be to be able to uncover the underlying mechanisms of neuromodulation that we anticipate will lead to more advanced, safe, and effective therapies. So, it's really stressing the challenge that there is very little understanding of the mechanisms of action of neuromodulation therapies. So what we hope to understand better through the funded programs and projects within SPARC is a better understanding of neuromodulation.

Next slide, please.

And so, as I've said, toward the end of the program, we will have sufficiently advanced neuromodulation therapies so that there is a more precise neural control of an organ system function.

Okay, next slide.

[SLIDE]

And many of you are probably aware that there are other parallel opportunities that are ongoing, certainly within the NIH, with other government agencies like DARPA, and certainly in the private sector with GSK. So GSK is the bioelectronics challenge, and then DARPA is the electric program, which parallels very much what the NIH SPARC program is doing. In addition, there is the NIH BRAIN Initiative, which is primarily focused on the central nervous system.

So what we have here are coordinated activities at the higher level so that there is a lot of cross-talk within all these different activities, and we're still in the process of identifying other opportunities where the funded activities will actually help sufficiently inform and better propel each of—the fields forward in a much more catalytic way.

Next slide.

[SLIDE]

In the next few slides, you will now hear from each of the program leads of the research components for SPARC. So first will be Jill Carrington, who will talk about the research component and the anatomical and partial mapping of innervation of major internal organs. And what we are seeking in

this component would be developing the anatomical and functional neural circuit maps for multiple organs with the deliverable being having developed novel electro-design surgical procedures and new stimulation protocols.

And then, next, Dr. Grace Peng will talk about the next-generation tools and technologies where projects that are seeking to develop novel and adaptive technologies for the peripheral nervous system will be awarded. And the deliverable here would be to develop the next-generation neuromodulation therapies.

Next, I'll go back and talk about the use of existing market-approved technology for market indications, and the activity here is really to in some ways reposition existing market-approved devices for new indications so that we can, at the end of the day, have new therapeutic opportunities and methodologies.

And then, lastly, Dr. Vinay Pai will talk about the activity toward the Data Coordination Mapping and Modeling Center, with the goal of creating a public data resource that would incorporate all the SPARC data with the end goal of having a query-able, integrative, and predictive anatomical and functional neural circuit maps.

Next slide.

[SLIDE]

This is a broad overview of the new mechanism that I talked about, so, essentially, SPARC will use essentially two award mechanisms. One is the Cooperative Agreement mechanism, which many of you are probably familiar with. The other one is what's called the Other Transactions, or Flexible Research Authority, and you can find out more information about this at the website that's indicated. But, basically, Other Transaction is better defined as the negative; that is, it's not a grant; it's not a Cooperative Agreement; it's not a contract. It's really intended to be an award mechanism that provides NIH and the awardees maximum flexibility in terms of the execution of the project.

And so the way this is going to lay out is that prospective applicants will submit an OT1 pre-application package that will then be reviewed. It's almost like a white paper. And so there's no money that will be awarded for the OT1 stage, but what it does is that if you're successful, then you'll be allowed to submit a full application, what's called the OT2 full application, that will then go into an additional review process, and if successful, awardees will be able to negotiate the benchmarks with NIH staff and then be able to then be issued the OT award.

What we hope to achieve here is that it will be a much more streamlined and flexible way where there will be an opportunity for NIH staff to be engaged and for revisiting program goals and even doing mitigating risk of the research.

And so Dr. Carrington will elaborate more on the Other Transaction process as it relates to her program on developing functional neural circuit maps. I'll turn it over to Dr. Carrington.

DR. CARRINGTON: So I'm going to be talking about the anatomical and functional mapping of the innervation of major internal organs. And, currently, we have announcements that are either active or in process already for two types of projects. The first type of project is ongoing on comprehensive functional mapping of neural anatomy and neural biology of organs. And this is through the Other Transactions mechanism, and so we're working through OT1 pre-applications and OT2 final applications. The OT1 applications have already had two receipt dates in 2016, and then we have continuing receipt dates every two months through January 2018. This announcement is for projects that use multi-expertise approaches to comprehensively map neural control circuits for organ function. There are specifics that are found in the RFA in terms of what we're looking for and what we're not looking for. These are three-year projects with up to $2 million per year in direct costs.

And I still hear a lot of background noise. Are you getting me, Grace?

DR. PENG: Yes, I can hear you, but I would appreciate it if the others can mute their lines.

DR. CARRINGTON: Okay, and the second type of project [inaudible 17:01] phase, so it's a limited competition based on the OT1 applications we received. And this component really is to help people to answer critical questions that may need to be addressed before a comprehensive mapping project can be planned in order to understand the [inaudible 17:27].

Can you change to the next slide, please?

[SLIDE]

DR. CARRINGTON: We're still getting a lot of background. I can hear people having conversations in the background.

In terms of the announcement for comprehensive mapping projects, please note that there are specific instructions for the OT1 pre-applications in several [inaudible 18:01]. Note that we're asking for a 1-page specific aims, and then you have a 12-page research strategy section. And, Grace, can you continue with the slides, please?

So we ask you in the background in significance to briefly describe the major knowledge gaps and the barriers for neuromodulation of the proposed organ on which you're focusing, along with how this project will fill those information gaps to enable effective neuromodulation therapy. We do ask for benchmarks and deliverables, and a timeline for the project.

And, Grace, you can continue on down.

We do ask for information on the investigator expertise and how that will be filling a need in the project. We do not in the pre-application phase ask for budget pages, but we do ask for a total direct cost

estimate for each year so we have some idea of the ballpark. And this is not something that you're tied to in the OT2 application, but we want to have some idea of the cost of the project.

And you can continue, Grace.

And it's an option to highlight the conceptual, technical, and/or methodological innovations that you might need from other investigators for the proposed project within SPARC.

And go ahead, Grace.

We do not require letters of support for the OT1 pre-application, but please do note that for the OT2s you have to have successfully been reviewed at the OT1 phase and received an invitation to submit in the limited competition OT2. And then we do require a resource-sharing plan. You should read this information carefully. All applications have to commit to making data, biomaterials, models, reagents, tools, resources, methods, and SPARC-developed technologies usable and available to the other SPARC projects, including the SPARC Data Coordinating Center and more broadly to the research community.

So those are some of the highlights in the research strategy section. We would recommend that prospective applicants read both the OT1 and OT2 RFAs before applying for the OT1. I am available and will continue to make myself available to people who are interested in applying to this for conversations before submitting an application if you have any questions about the announcement. Please do pay attention to the review criteria, which for these OT applications are different from the usual R01 review criteria at NIH. And also note that the review criteria for the OT1 phase and the OT2 phase are different from each other. And so keep that in mind as you are working through these applications.

And I'm sorry if there was interference and some of that presentation got missed by some of you. So, please don't hesitate to send me an email and let me know if you have questions. I'll be happy to follow up with any applicants.

And now I'll turn it over to Grace.

[SLIDE]

DR. PENG: Thank you, Jill. So I am going to talk about the technology funding opportunities for SPARC. And I just wanted to make mention that we were able to fund 12 U18 projects in September of last year, and these projects are working hard at developing new technologies for SPARC.

If you go to our SPARC website, the front page, which is listed here on the bottom right corner, there's a great table with icons on it. And you can click on any of those icons to show you the projects that are being funded. And the table tells you which categories of technology and what organ systems they're focused on.

So these awardees are working hard and setting up the stage for future awardees for SPARC to work on how to share among the SPARC awardees. So that's a very exciting activity that's going on.

So, as a next step for the technology funding opportunities, we have released an Other Transaction Authority mechanism for funding for technologies to understand the control of organ function. So it's very similar—for those of you who saw the U18 RFA, this is very similar in the types of technologies we're trying to support here.

Again, as Dan mentioned, we are in the first phase of SPARC for discovering the mechanisms of action of the peripheral nervous system. And so the purpose of these technology initiatives is to develop new technologies to assist in the discovery of the mechanisms and not for neuromodulation therapies.

The next receipt date is the last receipt date. We already had two—we have two receipt dates for the Other Transaction Authority technology funding opportunities, and the next and last receipt date is May 16th of this year. So we would encourage you to think about applying if you do have some technology you're thinking about developing.

So, again, these are tools and technologies for elucidating the underlying neural biology and neural physiology for autonomic control of organs in health or disease. And you are supposed to tailor your technology development toward the organ or organs of interest.

[SLIDE]

So, again, as Jill did, I will show you the example for the OT1 application. In section 4 of the RFA, it gives you the guidelines of what applicants should submit. And the purpose of showing this is to let you know that it's really not a burdensome application. It's six pages. Again, the aims are indicating how your technology project will contribute to advancing neuromodulation science related to the organ of focus. We're asking you to provide up to two pages of impacts and significance of your technology development and how your technology will overcome any gaps or knowledge gaps brought by the biology community in understanding the peripheral autonomic control of an end organ.

Preliminary data actually is optional. Only if you have it, you can include up to one page. Benchmarks and timelines—up to two pages; again, it's to give us an idea of the different steps and processes in the tasks that you would like to do for this technology proposal.

Investigators, again, we're saying that you pretty much list your expertise in a table in one page so we know what kind of investigators are part of your team for developing the technology. The budget, in total with the direct cost estimates per year, and letters of support are not required for the OT1 pre-application. And we do require that you commit to making all the tools that you're developing through this technology project available and useable by other SPARC projects. So it's, again, following along the same philosophy in which these projects are no longer just a project for your laboratory or to promote the research in your lab but it's really to go toward this greater effort of building a SPARC community and creating a legacy in which your tools will undermine the mechanisms—determine the mechanisms for autonomic control of organ function, and that ultimately will be delivered to the SPARC community.

So I think that's it for now for what I have, so hopefully this OT1 application, again, as Dan mentioned, will be reviewed and then you'll either be recommended to move on to the OT2 application—those of you who submitted to the first OT1 receipt date will have the opportunity to come again for thinking about possibly submitting for the May submission date.

[SLIDE]

So I will go on to the next slide, which I think is Dan's opportunity.

DR. TAGLE: Thank you, Grace.

So the third component of SPARC is on preclinical development of existing market-approved devices. And this is to support new market indications. Unlike Jill and Grace's components, which are using Other Transaction Authority, this is a Cooperative Agreement mechanism, as indicated by the U18, which is the award mechanism being used.

Just to highlight that the receipt date for this is May 2nd and then draw your attention to the RFA number, RFA RM16-002. So the goal of this component is to use existing neuromodulation devices that have been market approved. And what SPARC will do is support preclinical testing toward new market indications.

Now, what is key in this program or this component is that SPARC has already established partnerships with a number of device manufacturers, and those are indicated in the device portal. And that's shown in the next slide.

[SLIDE]

So we have a number of device manufacturers: Boston Scientific, Medtronic, CVRx, Ripple, and Blackrock, and they have made available a list of devices that you can find at the device portal. Essentially, the application process would involve the applicants taking a look at the device portal in terms of what market-approved devices are currently made available by the partners and then contact the individuals listed under each of the companies. So that would be Stephen Carcieri at Boston Scientific, Tim Denison at Medtronic, Seth Wilks at CVRx, and also Danny McDonnall from Ripple, and Brett Dowden from Blackrock. So contact them, indicate what new market indications you would like to have for the devices that you are interested in.

And, essentially, we have also provided template agreements. These are NIH template agreements that the applicants can use in terms of their interactions with the device manufacturers. So we have a CDA, Confidential Disclosure Agreement, that would allow the device manufacturers to disclose more information about the device, and you can then use that information to inform your application.

If the proposed project has a lot of traction with the device manufacturer, that would lead to the establishment of a Collaborative Research Agreement, a CRA, between the applicant and the device

manufacturer, and even though that does not necessarily need to be in place by the time the application is submitted, we will certainly require that the CRA be established by the time the award is made.

What is also key in this U18 Cooperative Agreement mechanism is that it is milestone driven. And so it will be required that you have healthy, quantifiable milestones by which to benchmark your progress in this two-year award process.

So, next slide.

[SLIDE]

And so, just like Jill and Grace, I'll elaborate more on Section 4 of the RFA. And so the SPARC application for the U18, using the U18 mechanism, is 12 pages. Letters of intent are optional. Essentially, in your background information you need to describe the current state of knowledge and the etiology and clinical characteristics of the new indication that you're proposing to study, along with the current and projected prevalence and the limitations of existing therapies. For the significance, it would be important to state the scientific reasoning for the proposed therapeutic effect of the stimulation at the chosen site, including how stimulation modulates peripheral control of end organs, function, and certainly the implication of the specific indication being addressed.

As I have said, milestones would be a key part of this process, so it would be important to state quantifiable milestones with clear go, no-go criteria. And, certainly, it would be helpful to also have a Gant chart that indicates where in the two-year timeline those milestones are to be met.

Letters of support: if the CRA is not yet in place, certainly a letter of support will be required for the U18 submission. And then, in addition, we will also require a resource-sharing plan from the applicant, which would essentially stipulate timely data release to the SPARC Data Coordination Center.

As I have mentioned, the CRA needs to be established by the time the award needs to be issued.

And then I'll turn it over to Vinay.

DR. PAI: Thank you. As Dan, Grace, and Jill have mentioned, the three components of—Grace, if you could click it forward….

[SLIDE]

So what we all have been insisting here is that we need to see a lot of collaboration and tight communication between the various components of the SPARC program, which is indicated by these color-coded arrows.

If you can click one more….

What we also expect to see is that we have a fourth component, and this is the Data Coordination Center, the plan for this Center is that it will be a central informatics resource for the entire program and will enable the information about SPARC and results and conclusions from the overall SPARC program to be made available to the wider scientific community.

The plan is that it will work in tight coordination with the three components and integrate results and data from these components. Additionally, the plan is to produce a very detailed, integrative, predictive functional and anatomical neural circuit map of the autonomic and sensory innervation of the multiple internal organs or organ systems.

The approach we're using is this way because we want to make sure that when we've done the neural circuit maps, researchers and clinicians can use these maps to improve how they develop and test new electrodes and new stimulation protocols or modify protocols that are existing, and also for developing approaches for minimally invasive surgical procedures for neuromodulation.

And so, as you can see from these arrows, there's an intent from NIH and from the community for these kind of tight collaborations across all of the components and data sharing to a large extent.

Click it forward.

So, additionally, as I said before, the Coordination Center will also be a scientific resource, but the main collaboration will be coordinated and managed by the NIH program staff and the project team actually led by the SPARC Program Manager.

Next.

[SLIDE]

Finally, the contacts and resources that we have: the main coordinator right now for the program is Dan Tagle, who you just heard from. The project is led by four different leads. For the biology, it's Dr. Jill Carrington. For technology, it's Dr. Grace Peng. And for the new market indications, it's Dr. Dan Tagle and myself. I'm leading the data coordination as well.

The whole program is being directed through the Common Fund, which is—the program is led by Mary Perry of the Common Fund. And Kristina Faulk is coordinating the communications for us.

We have emails and phone numbers here, and you can click on the website to go and check more details about the program and any new funding announcements that we will have.

Thank you. Grace?

DISCUSSION

DR. PENG: I'm going to unmute everyone to open this up for questions and answers. So, again, if there is noise on the line, we'll see who the noise is from, if you can just mute yourselves.

Okay, everyone is unmuted. I think there is also a question on the Q&A already. I think Dr. Poon asked: Is the focus on stimulating peripheral activity meant to exclude inhibiting peripheral activity?

I think your question was up if you want to voice it. Dr. Poon, are you on the line?

DR. POON: Yes, I am.

DR. PENG: Your question was cut off in the chat box if you want to verbalize it.

DR. POON: Oh, is it? So my question is whether the focus on stimulating peripheral activity is meant to exclude inhibiting peripheral activities that are already active or maybe even hyperactive.

DR. PENG: Jill, did you want to answer that?

DR. CARRINGTON: Sure. So, no, we're not excluding inhibitory activities at all. I think the stimulating really refers to perhaps what electrodes might be doing more than what the nervous system is doing. So, at this phase, at least for the biology projects, we are interested in both afferent and efferent innervation of a single organ, and in understanding how that innervation is regulating the organ, whether it's stimulatory or inhibitory of organ function or whether the innervation itself would be a stimulatory or inhibitory signal is still of interest.

DR. POON: So, a further question, if I may. Is that you indicated that the use of electrodes for stimulating—would there be a possibility of other ways of modulating nerve activities, not necessarily by electrodes or stimulation, but by some other means, maybe physical means or chemical or pharmacological means. Are those being excluded, or is this only electrode stimulation?

DR. CARRINGTON: No, I'll let Grace also answer that from the technology perspective, but, for example, at our workshop, we had discussions of multiple approaches to regulating nerve activity and organ function.

DR. PENG: That's correct, and I just opened up the technology FOA, and we do have a list of the different technologies we're interested in for discovery. But, as Jill said, if you're not developing technology and you're using technology and you're interested in mapping, you can use different types of mapping technologies. But in the technology RFA, we are supporting the development of new types of technologies.

You can see here in these bullets—for those of you who can't read your screen, you can double click on the shared screen and it will become full size on your screen. So we are open to all sorts of sensing and stimulating types of technologies. And I just want to emphasize that this OT funding opportunity actually has been expanded in the types of technologies we're looking for beyond the U18 call. If you had read the U18 call, this particular call has expanded to multiple organs for stimulation and recording. So I encourage you to take a look at this Section 1 of the technology call.

DR. MUSHAHWAR: Grace, Vivian Mushahwar here. Maybe I can just follow up with a question on the technology portion. Did I understand correctly that the last date for the OT2s is May 16 for this year, so, in other words, if you haven't gone through the OT1, this opportunity is not available until next year?

DR. CARRINGTON: No, so for—the next OT1 call for technology—I'm showing now the website of all of our funding opportunities and the dates on the right-hand column. The next OT1 call for technology is May 16th.

DR. MUSHAHWAR: Got it. Okay, thank you.

DR. CARRINGTON: Sure.

UNIDENTIFIED: This is [inaudible 41:08]. A follow-up question for that is: there was a limited number of partners NIH has. If someone has other kinds of partners, can NIH consider additional companies to be included in that list?

DR. PAI: Yes, the NIH is willing to consider additional partners. In fact, that's indicated in our website that we welcome additional—in addition to the five that we have—any companies that you're aware of or that you can encourage to participate if you're interested in a particular device that they may have.

UNIDENTIFIED: Thank you.

CHARLES [INAUDIBLE 41:49]: Dan, this is Charles [Hornet-Pit ? Inaudible].

DR. TAGLE: Yes, hi Charles.

CHARLES: Hi; a question about the device portal site. I'm aware of the table, and it has four devices there. But Medtronic is not listed. Could you say more about what they're offering?

DR. TAGLE: We're still in the process of uploading that, and it should be populated by tomorrow.

CHARLES: Okay, I'll check it out.

BRIAN MCLAUGHLIN: I have a question for clarification. This is Brian McLaughlin. So, the OT1 process—once, if it's an application—and the next date you made clear a minute ago. And then it sounded like you go through the OT1 process and if that's accepted, then you're invited to submit an OT2 application, and so then funding would only come after essentially the two subsequent—or consecutive review cycles. Is that correct?

DR. CARRINGTON: This is Jill. I'm not sure exactly what you meant by the two consecutive review cycles, but what happens is the OT1 comes in and is reviewed according to the review criteria in those announcements. And then, yes, if you're invited to the limited competition for OT2, then the OT2 application is to come in and be reviewed, and then funding decisions are made following that review.

Does that clarify it?

BRIAN MCLAUGHLIN: It does. So then you would then apply at the next available funding round date for the OT2, so there's sort of a consecutive date that you ultimately need to apply for and undergo the review. Is that correct?

DR. CARRINGTON: Oh, I see. There are two separate dates to apply to, but the OT2 receipt date is set following the OT1 review. So you are notified of that receipt date.

BRIAN MCLAUGHLIN: Okay, and is there a separate scientific review as part of the OT2, or is that only Council review at that point?

DR. CARRINGTON: No, there is a scientific review and there are review criteria that are listed in that OT2 announcement as well.

BRIAN MCLAUGHLIN: Thank you.

DR. PENG: I just want to reiterate that the OT2 application receipt dates are not listed on this site, as you can see here. They will be—the applicants will be informed of their date of submission when they're invited to submit.

Are there any other questions?

DR. TAGLE: Yes, there was another question in the chat box I think.

DR. CARRINGTON: Oh, from Dr. Gregor—did you want to voice your question?

DR. GREGOR: Hi, sorry; I was just a little bit hesitant to use the microphone given some of the troubles we were having earlier.

Yeah, I was really just questioning—the terms look like preclinical studies, particularly for the U18 mechanism—if things that didn't involve autonomic systems and did involve work with human patients—if that would be considered responsive.

DR. PAI: Yes, so the intent of the U18 is actually to support the early-stage feasibility studies at this point. Any funding for the clinical part will actually come in the next round of solicitations, which we're still working on at this point.

DR. GREGOR: Okay, so I'm still not sure I quite understand. So that sounds like not human work then.

DR. PAI: Right, yeah, so nonclinical studies will only be the ones funded, and clinical studies will be a separate funding opportunity.

DR. GREGOR: Okay, that may come in the future.

DR. PAI: That's correct.

DR. GREGOR: So at this point you're only interested in *in vivo* animal work.

DR. PAI: Yes, for the—that's essentially what we want, because if it's a new market indication, then it's essentially proof of concept or feasibility studies that it actually will work prior to human studies.

DR. GREGOR: Okay, so if I think of a feasibility study, that's first-in-humans sort of work, when I use the words "feasibility study." Okay, thank you.

DR. CARRINGTON: This is Jill. I just want to add to that a little bit because you're talking specifically about initiative 3, and those answers really apply to that. So we also are not looking for clinical work in the comprehensive mapping project; however, you'll notice that we do require validation of data in human systems as a part of those projects. And so we also are not looking for clinical work, but we are looking for understanding of innervation of human organs as well, and so validating animal data will be an important part of those projects.

DR. MUSHAHWAR: Vivian Mushahwar again. Dan, I'd like to follow up on a question regarding the third initiative, the preclinical testing. Do you anticipate that this requires GLP type of work? Is that what you refer by preclinical testing, or is it proof of principle in animals?

DR. PAI: It will be certainly as close as possible to GLP.

DR. MUSHAHWAR: Okay, got it. Okay, I think I should read those more carefully. Thanks for pointing that out.

[UNIDENTIFIED 48:25]: I have one quick question. On the technologies and tools, is there any guidance on the sort of—I guess budget planning might be the way I would put it? I know no budget is required at the OT1 stage, but is there any guidance on the scope of the technology, what that should be in view of an OT2 application?

DR. CARRINGTON: So I've opened the OT2 for the technology RFA and we do have a special section on the budget. I'm just trying to find the budget here. And so we have provided an estimate of your budget to be between $250K to $300K in direct costs per year up to two years, but we do have a special note that because this is an Other Transaction mechanism, these awards will have the opportunity for supplemental funding should you need to extend the budget in duration or in amount. And so the OT mechanism is supposed to allow for maximum flexibility and fluidity based on the needs of the projects. So I would take advantage of the OT1 application to talk about what would be ideally needed for your budget. You could talk about the different levels of funding. That might be helpful in what we would get out of it in terms of the different types of technology that you could produce in two years and deliver for the SPARC community.

DR. PENG: Are there any other questions?

If not, on behalf of the SPARC project team, we thank you for participating on this call. We will be archiving this recording once it's transcribed and accessible to all viewers. And so expect that this recording will be available in the next few weeks on the SPARC website.

So thank you all for participating. I'll adjourn the meeting now.