



National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Pre-Application Meeting for Physical Science-Oncology Centers (RFA-CA-09-009)

January 23, 2009

Natcher Conference Center (Building 45), NIH Campus, Bethesda, MD

Meeting Logistics and Agenda

Jerry S.H. Lee, Ph.D., Center for Strategic Scientific Initiatives, National Cancer Institute, NIH

The meeting was called to order at 10:00 a.m. ET by Dr. Jerry S.H. Lee, who along with Dr. Larry A. Nagahara, serves as program official for this RFA. He informed attendees that he would serve as moderator for the meeting and welcomed everyone's participation. Dr. Lee reminded web-attendees that there was a simultaneous viewing of slides via Adobe Connect and to sign-up at <http://physics.cancer.gov> to receive program updates, reviewed the meeting agenda, and then introduced Dr. Anna D. Barker.

Introductions

Anna D. Barker, Ph.D., Deputy Director, National Cancer Institute, NIH

Dr. Barker welcomed all of the attendees and acknowledged the contributions of Drs. Lee and Nagahara in bringing this initiative together. She also acknowledged the other presenters, including Ms. Amy Knight from the NCI's Office of Grants Administration and Dr. Kenneth Bielat from the NCI's Division of Extramural Activities. Dr. Barker then introduced Dr. John Niederhuber, Director of the NCI, who is also a nationally known surgeon, accomplished clinician, and dedicated bench scientist. She noted that Dr. Niederhuber has been very supportive of this initiative.

Welcome and Opening Remarks

John E. Niederhuber, M.D., Director, National Cancer Institute, NIH

Dr. Niederhuber welcomed everyone to the meeting and gave special thanks to Drs. Lee and Nagahara for their work on this RFA. He also acknowledged the National Cancer Advisory Board (NCAB) and the NCI's Board of Scientific Advisors (BSA) for their input and enthusiasm. He noted that a little over a year ago he discussed with Dr. Barker the idea having interactions between oncology and the physical science experts. As a result of those discussions, a series of very exciting meetings were held in 2008 with the goal of bringing physical science experts together to ask them how they would deal with the very complex challenges of cancer research. At those meetings, and here, Dr. Niederhuber challenged participants to create something unique that would change the way cancer is viewed, acknowledging that his role would be to find the resources to support the innovation.

Question: Is this new direction a long term change for the NCI?

Answer: Whether this new direction is productive and successful will be carefully measured. It will be as long term as it is successful. It will grow if it should grow, and it will terminate if it is not successful.

Opening New Frontiers: Physical Sciences in Oncology

Anna D. Barker, Ph.D., Deputy Director, National Cancer Institute, NIH

Dr. Barker noted that the RFA is open ended in terms of a submitter's ability to innovate and think outside the box on how these fields could converge to help advance against cancer. She also expressed a few take home messages:

- This initiative is not just about creating interesting science. This is about opportunities for real exponential change in the war on cancer. So, the NCI is looking for really good ideas to be brought to the table.
- Creativity and thoughtfulness will be important while putting applications together. The submitters are being asked to focus around an organizing framework that utilizes a physical sciences-based approach to tackle a major cancer question/barrier.
- Submitters are encouraged to be creative in developing these organizing frameworks and to trust that the NCI will do its best to recognize and support such innovative thinking.

In her presentation, Dr. Barker began by describing the general S curve of science—starting with empirical observation, followed by a subsequent data explosion, the rise of partial theories for complex systems, and then finally a search for unifying theories. She argued that several NCI programs are already engaging along that S curve right now, where projects such as The Cancer Genome Atlas (TCGA) and the Tumor Microenvironment Network (TMEN) are producing an explosion of new data, the Integrative Cancer Biology Program are developing partial theories for complex systems, and this new initiative, the Physical Sciences-Oncology Centers (PS-OCs) will serve a key role in the NCI's search for unifying theories.

Dr. Barker provided brief highlights of the series of meetings that were held to explore the potential of using physical sciences to open a new frontier in oncology. More than 300 physical science and oncology experts met around this issue over the course of 2008 and discussed a range of issues and barriers facing cancer across different length scales. Four consensus scientific themes emerged from these meetings and were incorporated into the RFA to stimulate creativity in developing PS-OC organizing frameworks, including:

- Understanding the physics of cancer
- Evolution and evolutionary theory in cancer
- Coding/decoding/transfer of information
- De-convoluting the complexity of cancer

She noted that if submitters have better themes around which to organize their projects, they are encouraged to propose them.

Question: In terms of innovative thinking and thinking outside the box, what is expected and what would be the measure of success?

Answer: The hope is that in the early stages of this initiative, the desired teams will begin to both talk with each other to exchange information and to create new concepts and hypotheses that can be tested. Beyond that, the goal is for scientists who are cross-trained in these disciplines to create new convergent fields and “schools of thought”. What the NCI is looking for is real advances that can substantially mitigate the problem stated in each PS-OC's organizing framework. A large number of metrics will be used to gauge success, ranging from very specific kinds of criteria in terms of what is proposed in the project, to determining whether the project contributes to building the PS-OC's community and advancing the center's new thinking.

Participant Follow-Up Comment: There are two possible ideals that may come from physical scientists. One deals with specific scientific mechanisms, like energy. The other is how physical scientists approach and solve problems. Given all this and given that there is a whole range of biological information, the challenge is taking the physical ideas and incorporating all the biological information.

Answer: That states perfectly the intent of the RFA. As physical scientists look at the problem with a different perspective, the hope is that the physical sciences will drive the way the questions are formulated. The integration of information will follow if the organizing framework is sound. It's a huge challenge.

PS-OC Program Goals and Objectives

Larry A. Nagahara, Ph.D., Center for Strategic Scientific Initiatives, National Cancer Institute, NIH

*PowerPoint slides for this presentation can be found [here](#). The highlights and additional information included below are meant to supplement the slides.

(Slides 1-2)

The specific purposes of the PS-OC initiative are:

- To generate new knowledge and catalyze new fields of study in cancer research by utilizing physical sciences/engineering principles to enable a better understanding of cancer and its behavior at all scales.
- Not to build new tools to do “better” science, but to bring new perspectives and approaches to do paradigm-shifting science that could lead to exponential progress against cancer.
- To build trans-disciplinary teams and infrastructure to better understand and control cancer through the convergence of physical sciences and cancer biology.

The vision for the PS-OC network is:

- Creating a collaborative network consisting of virtual centers that focus their individual efforts around an overarching organizing framework.
- Bringing together subject matter experts from the physical sciences and oncology to create new schools of thought to address the major barriers/questions in cancer with a physical science-based approach

(Slides 9-10)

An example of how to potentially structure a PS-OC was presented:

- Organizing framework: For example, the theme could be understanding the cause and effect of metastasis *via* the integration of physics (physical laws and principles) and cancer biology. This could include defining the role(s) of thermodynamics and mechanics in metastasis and determining how this knowledge might be employed in new intervention strategies.
- PS-OC structure around the framework: In this example, the three areas contributing to the organizing framework could include:
 - Project 1 – thermodynamics and metastasis
 - Project 2 – mechanics and metastasis
 - Project 3 – mechanic/thermodynamics and intervention
 - *etc.*
- Shared Research Resources (SRR). Two SRRs might be used for the projects including:
 - Computation facility (which may be used in Projects 1 & 2)
 - Cell line/mouse model core (which may be used in all projects)
- Administration Unit, Pilot Projects, and Trans-network Projects. These units would be as described above.
- Outreach/Dissemination Unit and Education/Training Unit would have the purpose of developing a pipeline of new researchers

Question: How tightly should the projects be coupled to the framework?

Answer: The projects need to support, demonstrate, and advance the PS-OC’s organizing framework.

Question: Do you foresee any translational research in the Centers?

Answer: Eventually. The ultimate goal is the clinic, but NCI realizes that this may not be reached in the first five-year award term.

Question: Would there be any preference towards proposals that address specific cancer types?

Answer: While a specific model may be used for specific projects, a broader understanding of a major barrier/hurdle that is potentially applicable to all cancers needs to be the ultimate goal of an organizing framework (please see RFA for exact language).

Question: To what extent can a submitter create a hybrid theme, or one that does not directly address anyone of those particular themes?

Answer: As stated previously, and in the RFA, it would be appropriate as long as the organizing framework is scientifically justified and addresses a major barrier/hurdle in cancer using a physical science-based approach.

Question: It sounds like the three to five projects requirement is set in stone. Is there any flexibility in going to either side of the range?

Answer: No, but the projects may have varying sizes.

Question: If an institution has both a strong physical science program and a strong cancer biology program, can the requirement to collaborate with additional institutions be ignored? And, if so, to what degree?

Answer: No, but how the additional institutions are engaged is up to the submitters. Please note that the NCI's BSA recommended that we include this requirement for collaboration.

Question: Are there any expectations in terms of the number of investigators from each collaborative site?

Answer: That will be left up to the submitters.

Question: Subcontracting between institutions leads to a tremendous loss of funds and a bottleneck for bureaucracy. How will this be addressed?

Answer: Mechanisms to help minimize the costs and bureaucracy have been discussed with NCI Office of Grants Administration (OGA). These will be discussed in presentations this afternoon.

Question: Could you say more about development of new tools? What if one is needed?

Answer: To expand upon the statement made in the presentation, while the intent of this program is not the development of new tools, if a needed measurement to support the organizing framework requires a new tool, it would be appropriate to propose one.

Question: Will it be acceptable to the reviewers if the majority of the best proposals focus on the same theme (like evolution), or will there be an attempt to accept projects across the array of themes?

Answer: The NCI believes that there will be good ideas proposed in the four suggested theme areas, and others if justified. We have extensive experience ensuring that there is balance across the network through careful analysis of summary statements and the development of appropriate funding plans.

Question: Regarding the individual projects, are they expected to be in the R01 format, or is there flexibility to be creative in terms of, for example, reporting preliminary data?

Answer: In short, yes, and we have received several questions around preliminary data prior to this meeting. Please check the FAQ site (<http://physics.cancer.gov/RFA/RFA-CA-09-009-FAQs.asp>) for an expanded and more detailed response to your question about preliminary data.

PS-OC RFA Component

Larry A. Nagahara, Ph.D., Center for Strategic Scientific Initiatives, National Cancer Institute, NIH

*PowerPoint slides for this presentation can be found [here](#). The highlights and additional information are included below are meant to supplement the slides.

(Slides 2-3)

- Key dates — the Letter of Intent (LOI) receipt date is **February 13, 2009**. The receipt date for the actual application is **March 13, 2009**.
- LOI submission — submission of an LOI is **highly encouraged**. The preferred method of submission is electronically, either in Microsoft Word or Adobe PDF document form. Additional recommended elements to help facilitate the review process include a brief description of the PS-OC organizing framework (three to five sentences). Relevant expertise and keywords should be included.

(Slide 6)

- Application submission — The multi-project application must be submitted in **hardcopy** form and should be **assembled and paginated as one complete document**.
 - Table of Contents (TOC) — It is highly recommended that applications follow the sample format style that may be found at <http://physics.cancer.gov/RFA/RFA-CA-09-009-FAQs.asp>

Preparing the PS-OC Application: Process and Suggested Format

Amy S. Knight, Office of Grants Administration, National Cancer Institute, NIH

*PowerPoint slides for this presentation can be found [here](#). The highlights and additional information are included below are meant to supplement the slides.

The role of OGA here is to help submitters put together applications in the proper format to work through the peer review process smoothly. If reviewers have difficulty locating information, an application score could be impacted negatively.

(Slide 3-4)

- Additional funding information — Direct cost caps are exclusive of consortium indirect costs. Budgets may allow for up to a 3% cost of living increase each year up to the direct cost cap, and should include any necessary costs in preparation for semi-annual progress reports.
- NIH budget caps to remember — The current salary cap is \$196,700 (Executive Level 1) and the current graduate student compensation cap is \$36,996.

(Slide 7-8)

- Form Page 1 and 2 are required for each project/core and should include the title and the name of the project leader. Signatures of business officials are required only for the main Form Pages for the entire application.

(Slide 10)

- Separate first year and cumulative budget pages should be submitted for each project, core, unit, and entire consortium.

(Slide 11)

- The individual center administration budget for activities such as progress reports, site visits, travel for CAC and PSC should be included under overall PS-OC Administration in Section N3: Center Organization and Infrastructure. **Separate budget pages should be prepared for CAC and PSC set-asides to support pilot projects and trans-Network projects, respectively.**

Peer Review Process for PS-OC RFA

Kenneth L. Bielat, Ph.D., Division of Extramural Activities, National Cancer Institute, NIH

*PowerPoint slides for this presentation can be found [here](#). The highlights and additional information are included below are meant to supplement the slides.

Dr. Bielat and Dr. Jeffrey DeClue are the Scientific Review Officers (SROs) designated to the review of this initiative.

(Slide 5-8)

- Additional review criteria listed in the RFA will be applied to the review of applications. The reviewers will be asked to pay close attention to these criteria which broadly include:
 - [Review Criteria for Overall PS-OC](#)
 - [Review Criteria for Center Research Projects](#)
 - [Review Criteria for Shared Research Resource Cores](#)
 - [Review Criteria for Education and Training Unit](#)

(Slide 14)

- To ensure the ability to find expert reviewers, **please do not name external advisors** in the grant application and **do not contact candidates** prior to submission.

Question: Will the slide presentations be available after the meeting?

Answer: Yes. The slide presentations from today's meeting will be uploaded to the FAQ site (<http://physics.cancer.gov/RFA/RFA-CA-09-009-FAQs.asp>).

Question: In terms of the budget, it was said that there will only be one signature on the face page. However, are additional signatures required when there are sub-contracts with other participating institutions?

Answer: Yes, this was to avoid redundant signatures for the awarded institution on the subsequent project/core cover pages. A signature is still required for each consortium activity outside of the awarded institution as stipulated by PHS398 instructions. This was meant only to reduce the number of identical and/or repetitive signatures. Please contact NCI OGA for additional information.

Question: There is a concern within the physical sciences community that ultimately, the applications will be reviewed by an NIH panel, with NIH expectations. How will the NCI ensure that this is not the usual review process?

Answer: The NCI Program Officers have had extensive dialogue with the Scientific Review Officers (SROs) and will continue to have these dialogues to ensure that the physical sciences view is reflected as much as possible in the review process. The SROs are also communicating this perspective to potential reviewers. At this stage, it is impossible to provide numbers for the various disciplines that will be required. The SROs will recruit reviewers based on the expertise required by the applications. The SROs strive to be fair to all applicants, even if it means bringing in reviewers by telephone for just one project. Please trust that the SROs have extensive experience in multi-component review.

Question: Is there any way to ensure that reviewers will be open minded about the subject of these proposals?

Answer: Significant effort has been put into identifying reviewers with the necessary expertise. There can be error, but this is minimized by using reviewers that have the relevant expertise, and that have been reviewers in the past. During the pre-review orientation teleconference, the initiative and what is expected of the reviewers is discussed. Prior to the review starting, the SROs will also re-iterate what is expected.

Question: How will the reviewers be selected?

Answer: It will depend on the nature of the application. It is anticipated that there will be a broad range of scientists representing the physical sciences, as well as representation from cancer biology and clinical oncology, as needed.

Question: How important will a track record of national funding be for submitters to show credibility in the eyes of the review panel?

Answer: Applicants must demonstrate that they are capable of conducting the proposed research. A good granting/publication record would be taken into consideration but would not be the sole metric used. The key point to keep in mind: is this the investigator that would be likely to get the job done?

Question: What is the perception of the NIH and peer reviewers on how much emphasis will be put on clinical translation components?

Answer: As stated previously, although translational research is welcomed, it is not expected that PS-OCs develop clinical interventions in the short term.

Question: Since this is cancer, and cancer occurs in organisms, will an animal component to the projects be necessary?

Answer: This harkens back to the discussion of supporting and substantiating the organizing framework. There is no preference for how applicants should demonstrate their models, but they should support and advance the PS-OC's organizing framework.

Question: With respect to the subcontracting barrier issue, if there are collaborations with outside investigators, how will that be taken care of from the sub-contracting end?

Answer: The work that is to be done at each organization in the PS-OC should be clearly stated with a separate budget, and so that when the applications come to the committee for review, there are separate applications for each organization that cross reference each other. Please note that the NCI does not pay overhead to a prime contractor on subcontractor's overhead. Generally overhead is allowed on a subcontract for up to the first \$25,000, which allows for administrative costs to be handled in setting up the consortium agreement, and the remainder of the indirect costs for the subcontract would be excluded from the indirect cost calculation for the prime contractor's institution.

Question: What is your guidance on how to design compelling trans-network research without knowledge of the network?

Answer: As described in the RFA, we are not asking you to propose trans-network projects at this time, but rather to propose and develop processes, mechanisms, and strategies for how these projects will be developed after award and include a standard set-aside budget as described by OGA previously. This is also the case for pilot projects. Both pilot and trans-network project proposals will be generated after the PS-OCs are awarded.

Question: Will each application be reviewed as a whole, or will it be taken apart and given to different reviewers?

Answer: There will probably be 15 to 30 reviewers assigned to each application. Reviewers' expertise will be matched with expertise involved in the project to determine review assignments. The application will be reviewed as a whole, and then its individual components will be evaluated, just like any other multi-component project. This is why the construction of the framework is very important.

Question: The sample TOC provided states that there should be individual budgets within each section, such as each project and each core. Do we still want them up front as well? Would it not be redundant to have them in two places? Wouldn't it be better to do an overall budget upfront and then individual project budgets?

Answer: The upfront budget is a composite budget that summarizes all the direct costs, and so it would be a total for all personnel costs, one grand total for supplies, *etc.* all in two pages (the first page being the first year breakdown and the second page being the five year summary)

Question: Will there be one section for biosketches, or will they be broken down in each project (as currently stated in the sample TOC)?

Answer: The sample TOC is provided as guidance since there are page limitations for Biosketches set forth by instructions for the standard PHS398 application. It is, encouraged, but not necessary, to duplicate the biosketches in each of the projects/core to help facilitate the review process.

Question: How do we find additional collaborators/investigators?

Answer: Please use the Teaming Site that is part of www.physics.cancer.gov.

Question: The issue of translational research has come up several times; please clarify its role in this initiative?

Answer: Many NCI initiatives require a translational component. Although it is not a requirement of this initiative, if one is fortunate enough to have translation occur in his or her PS-OC during the life of this project, no one will object and would be viewed very positively. That said, it will not be used as an absolute metric for peer-review as compared to other NCI initiatives.

Question: What is JIT information?

Answer: JIT stands for just in time. For example, if humans are involved in your project, you do not need to apply for institutional review board (IRB) approval at the time of submitting the PS-OC application. If you are selected for an award, then IRB approval would be required, JIT. Another requirement is updated support information for key investigators obtained at the time of award.

Question: What is the follow up plan for applications, both approved and not approved? Will there be another RFA?

Answer: The NCI is a good steward of the public's money and so every initiative is reviewed. This initiative will be evaluated regularly by the NCI staff and advisory boards. If the PS-OCs are successful, there could be a number of satellite grants. Those who did not get funded would also be in a position to propose pilot studies with those who did get funded.

Comment (Review Staff): Those who have colleagues in the field, especially in the physical sciences, may want to alert them that if they are called to participate as reviewers for PS-OC applications, that they make themselves available. It has become increasingly difficult to recruit the necessary expertise for NIH study sections. The input from the community governs the quality of the review.

Comment (Program staff): The program officers are available to answer any questions. Please sign up at www.physics.cancer.gov to receive updates.

Drs. Barker and Lee thanked everyone for their participation.

The meeting adjourned at 1:30 p.m.