

National Cancer Institute
Process to Accelerate Translational Science (PATS) Working Group Report

A Working Group of the Clinical Trials and Translational Research Advisory Committee (CTAC)

September 2010

Executive Summary

The purpose of this meeting was to provide advice to the NCI on the implementation of Translational Research Working Group (TRWG)-proposed initiatives to develop Special Translational Research Acceleration Projects (STRAPs). The vast number of translational cancer research opportunities stimulated by basic science advances imposes the need to create a transparent, inclusive process to identify, prioritize and fund the most promising early translational research opportunities. STRAPs are the funding program proposed by the TRWG to accelerate translational cancer research to provide human benefit in the shortest period of time. The NCI piloted the Translational Research Acceleration Initiative with the Immune Response Modifier Pathway, from the prioritization process to the release of a call for applications for a STRAP. Taking this experience into account, the following recommendations are made.

The NCI PATS Working Group recommends to the NCI's Clinical Trials and Translational Research Advisory Committee (CTAC) that the NCI initiate an umbrella STRAP solicitation immediately to fulfill the urgent need to accelerate translation for patient and public benefit. The more complicated prioritization process should be initiated with the goal of incorporating it into the umbrella STRAP solicitation whenever possible.

The recommended implementation guidelines include:

- 1) The NCI Initiate an umbrella STRAP solicitation covering potential translational opportunities in all 6 TRWG pathways.
 - a. STRAPs should fund the translational research opportunities that are "ripe" for acceleration based on scientific quality, technical feasibility, and expected patient benefit or public health impact.
 - b. STRAPs are discrete, time-limited, actively managed, milestone-driven projects directed at the goal of early stage human testing (Phase I/II trials).
 - c. The 6 TRWG pathways provide a roadmap for required steps, but flexibility to accommodate evolving approaches and projects that span pathways is required.
 - d. In order to provide maximum flexibility and rapid initiation of projects, STRAPs link and leverage multiple existing funded NCI programs and utilize multiple funding mechanisms (supplements, grants, and/or contracts). Representatives of appropriate NCI programs are informed and involved in STRAP processes as appropriate, and are appointed to specific STRAP project teams.

- e. STRAPs are likely to include multiple investigators, institutions, and disciplines, since optimum capability to implement all pre-clinical and clinical development steps are unlikely to reside at a single institution. Project teams can be coalesced in advance, with or without NCI assistance.
 - f. To avoid undue effort on the investigative community, applicants submit a 1-3 page preliminary concept for review; those concepts judged most promising by expert extramural reviewers result in a request to the investigator to submit a full application for potential STRAP funding.
 - g. The NCI or expert prioritization committees have the flexibility to modify/replace STRAP components proposed by investigators to provide optimal resources and expertise for the project.
 - h. STRAPs are coordinated and facilitated by NCI-provided project managers.
 - i. Successful completion of STRAP funding leads to seamless, coordinated handoff to an advanced Phase II or Phase III trial, and not renewed funding. This handoff should be an actively managed process.
 - j. Considerable resources have been invested in the NCI's Experimental Therapeutics (NExT) program. The NExT program has focused resources and methods for prioritization. At least for the initial few application cycles, STRAP proposals for the Agents pathway with therapeutic intent should be directed to the NExT program.
- 2) NCI PATS Working Group members will be consulted to determine the practicality and best method to form pathway-specific subgroups for prioritization of opportunities and selection of STRAPs in the Biomarkers, Imaging, Interventive Devices, and Lifestyle Alterations Pathways. If subgroups are formed, the goals of each subgroup may be unique and must be clearly defined. Goals could include these categories:
- a. Identify translational needs and opportunities to inform NCI and the community in general.
 - b. Select most important opportunities in the field for future STRAP solicitations within the umbrella structure.
 - c. Establish criteria for evaluating pathway relevant STRAP concepts/applications.
 - d. Recommend how any existing NCI programs should be included, and whether new standing services infrastructure programs should be established to support STRAP projects. All existing NCI programs are expected to help facilitate successful results from STRAP projects.
 - e. Facilitate outreach/education to the investigator community regarding the STRAP program.

Background

The purpose of the National Cancer Institute (NCI) Process to Accelerate Translational Science (PATS) Working Group is to advise the NCI and its Clinical Trials and Translational Research Advisory Committee (CTAC) on developing a way to identify and prioritize early translational science and provide input into unique funding strategies designed to accelerate the prioritized

projects. The NCI PATS Working Group grew out of the [NCI Translational Research Working Group \(TRWG\)](#) recommendation to identify a few high-priority translational research projects that are “ripe” for translation and provide the financial resources and the project coordination required to accomplish their goals more efficiently.

Although early translation at NCI is currently supported by a variety of funding mechanisms, the TRWG concluded that certain early translational research opportunities will arise that deserve a more actively managed, fully resourced development program, both because of their readiness for development from a scientific and technical perspective and because of the importance of their potential clinical and/or public health impact. Accordingly, the TRWG recommended that NCI develop a new translational research acceleration initiative designed to advance selected early translational research opportunities in a more coordinated, highly facilitated and timely fashion. The initiative was envisioned to result in a Special Translational Research Acceleration Project (STRAP) program with the following specifications:

- Focus on a few highly meritorious projects each year
- Identify existing resources that when linked accomplish a specific goal
- Provide additional resources and project coordination to leverage components
- Funding is milestone-driven and time-dependent
- Successful STRAPs will lead to hand off to a Phase III trial

The NCI piloted the STRAP concept with the [Immune Response Modifiers pilot](#). Several lessons were learned:

- The Request for Information (RFI) did not provide the information that was needed to allow identification of the best potential projects. As RFIs are not associated with funding and/or availability of resources they are unlikely to generate the submission of the best ideas or complete project plans
- The prioritization approach used for the IRM STRAP was a time consuming process that may not be warranted for all remaining pathways. It is important to develop a prioritization process that is sustainable, objective, and informed by a diverse set of external experts in the field for each pathway.
- A structured prioritization process like that used for the IRM prioritization has a benefit of resulting in a framework that allows for efficient modifications and updates in the future.

The NCI PATS Working Group members participated in one-on-one telephone calls in advance of the meeting. These calls were used to gather input on three topics: continuing need for a STRAP program; understanding of the STRAP concept in the investigator community; and approaches for identifying candidate STRAPs and prioritizing them for funding. The face-to-face meeting scheduled for February 2010 was cancelled due to weather, and reconvened in Bethesda, MD on May 10, 2010. The purpose was to consider the recent experience of the [Immune Response Modifiers pilot](#) and determine how to best move forward with the other TRWG Developmental Pathways.

Confirm Fundamental Assumptions

Issues Addressed

The first task addressed by the NCI PATS Working Group members was to reaffirm certain fundamental assumptions generated from the one-on-one calls concerning the need for a STRAP program and aspects of its implementation. The group was asked to consider the following points:

- Is there still a need for actively managed, fully resourced projects to advance high priority translational opportunities to human testing?
- Are current funding approaches insufficient to meet this need?
- Is a new targeted funding program warranted?
- Is there a need to increase the understanding of the STRAP concept in the community?
- Should funding be focused on filling gaps in ongoing programs in the initial years?
- Is project coordination assistance needed and should it be provided by NCI?
- Is inter-pathway competition for 2-3 STRAP awards each year still a useful plan?

Outcomes and Decision Points

The majority (17/19 members present) of the NCI PATS Working Group members strongly agreed that there is still an unmet need to identify, prioritize, fund and accelerate a small number of translational research projects, in a coordinated and integrated manner, from a validated discovery through early human testing. Current funding approaches are inadequate for this purpose. They endorsed proceeding with a STRAP-like approach with the understanding that “the devil is in the details”.

Points discussed

- STRAPs could start at any point on the Developmental Pathway (not only at top of a Pathway diagram) but need to end with early stage human testing.
- STRAPs should be actively-managed by the scientific community (the investigators doing the work) and NCI should play a more facilitation/navigator role.
- Coordination across existing NCI programs, the extramural community, and other entities such as industry, represents a considerable challenge. The need for dedicated project management is high and the knowledge and skill sets required for effective coordination diverse.
- In the initial years, STRAPs should be focused on filling gaps in ongoing programs.
- An important emphasis in STRAPS is to proactively go after best opportunity
- An important emphasis of the program is to achieve results with clinical impact. The handoff to later-phase clinical trials must be proactively managed.
- Effective prioritization is key, both within and across Pathways.
- The lack of motivation in the form of dedicated funding has hindered identifying candidate projects for a large-scale prioritization effort

Reaffirmation of the continuing needs of the translational science community led to the remainder of the day’s discussion on how best to address those needs.

Identifying Candidate Projects

Issues Addressed

The optimal approach to identify the best candidate projects was discussed incorporating the knowledge gained from the Immune Response Modifiers pilot. Ideas generated during the one-on-one calls were discussed. These ranged from using *Broad Calls* (seeking from the scientific community full development plans or proposals to fill identified gaps in a development plan) to a more focused approach of identifying specific *Grand Challenges* in advance by a group of experts. There was in depth discussion of whether to develop Pathway-specific approaches in contrast to a common approach across all Pathways.

Outcomes and Decision Points

After intensive discussion, the consensus of the NCI PATS Working Group was that an expeditious way to approach the problem was to draft an umbrella STRAP solicitation covering potential translational opportunities in all 6 TRWG pathways and not pursue at this time a Pathway-by-Pathway approach to STRAPs. However, proposals for the Agents pathway with therapeutic intent should be redirected to the NCI's Experimental Therapeutics (NExT) program (see below). For this Broad Call solicitation, it was suggested that investigators submit a 1-3 page concept for review. Those concepts judged most promising by reviewers would result in a request to the investigator to submit a full application for potential STRAP funding.

Points discussed with general agreement

- An umbrella solicitation would rely primarily on the community to make the collaborative linkages
 - Some NCI PATS Working Group members felt that there are investigators that grasp the complete developmental pathway, and others will figure out how to coalesce themselves when there are dedicated funds associated with doing so
 - Others felt that less experienced investigators also have much to offer and should be assisted in identifying essential capabilities (e.g. similar to FDA/investigator meetings)
- The need remains to proactively educate investigators so that more people understand the developmental pathways so they can participate in STRAPs
- A communication plan for the STRAP program/process should be developed and proposal submission from all who can meet the criteria encouraged
- At least at the outset, funding should be focused on projects that will make maximal use of existing resources with a focus on filling gaps in infrastructures and programs
- Submissions may come from individuals or consortia-like entities
- The existing TRWG pathways are useful but should not be restrictive; i.e., proposals that combine existing pathways or develop new pathways with well justified steps and early clinical trial endpoints should be considered
- Allow requests for existing NCI resources and capabilities to link within a STRAP project
- Initial concept review should involve extramural experts, although it was noted that considerable expertise exists within the NCI

- NCI and expert panels would work with investigators to refine proposals, including modifying or replacing project components, to optimize the development plan
- Full submissions should be reviewed by at least one Special Emphasis Panel-like bodies, depending on the technologies/pathways represented. This may include multiple Pathways and fields of expertise.

Current Standing Services Infrastructure Programs at NCI

Issues Addressed

There are many standing infrastructure programs at NCI that provide a variety of services that are relevant to steps in the TRWG Developmental Pathways. Other programs are funding mechanisms that support investigators with a specific expertise relevant to Pathway steps. Approved STRAP projects should ideally be given access to these services as needed. A presentation by Dr. Jim Doroshow, Director of the Division of Cancer Treatment and Diagnosis at NCI, mapped currently-funded components to the TRWG Pathways which informed NCI PATS Working Group members on the various NCI infrastructure programs available. Considerable group discussion focused on the ways to best utilize and leverage these existing components to fill gaps in a potential STRAP development plan.

Outcomes and Decision Points

NCI PATS Working Group members found the presentation to be informative and helpful to the issues at hand. The group generally agreed that the NCI Experimental Therapeutics (NExT) program addressed the majority of the steps proposed within the Agents Developmental Pathway for therapeutics. It was pointed out NExT did not exist at the time of the TRWG report and that NExT fulfills the majority of the TRWG's recommendation for the Agents Pathway in this regard. Therefore, any early translational research opportunity for an agent with therapeutic intent should be sent to the NExT program rather than submitted in response to the STRAP umbrella solicitation, with the understanding that this can be revisited if the community feels there are specific needs not being met via the NExT program.

Regarding the remaining 5 TRWG Developmental Pathways, the majority of NCI PATS Working Group members felt that the standing infrastructure programs relevant to those Pathways were still incomplete. However, the initial approach should be to leverage existing resources to support approved STRAP projects, rather than to generate new infrastructure programs.

Pathway-specific Prioritization Subgroups

Issues Addressed

As there are 6 TRWG Pathways (Agents, Biospecimens/Biomarkers, Imaging, Immune Response Modifiers, Interventive Devices, and Lifestyle Alterations), the NCI PATS Working Group spent some time discussing whether or not it would be beneficial to develop Pathway-specific prioritization subgroups. It was noted that the first pilot only addressed the Immune Response

Modifier Pathway. If Pathway-specific groups are developed, consideration needs to be given to the proposed subgroups responsibilities. Examples include developing a prioritization process and criteria tailored to meet the needs of a particular Pathway and/or serving as a pool of experts for future review and prioritization of proposed projects. In addition, should subgroup formation be staged? If so, which ones should be constituted first and why?

Outcomes and Decision Points

NCI PATS Working Group members had mixed viewpoints regarding the need to form specific Pathway subgroups to reach the goal of prioritizing those translational research opportunities most “ripe” for acceleration. It was agreed that a “one-size-fits-all” approach is not appropriate. A way forward that was identified was to consult members of the NCI PATS Working Group representing the Biomarkers, Imaging, Interventive Devices, and Lifestyle Alterations pathways to determine if a Pathway-specific subgroup is warranted for their respective Pathways and, if so, to develop a defined list of goals and responsibilities for their respective subgroups.

Points discussed

- Goals of any Pathway subgroups could be varied and include:
 - Identify translational needs and opportunities to inform NCI and the community in general
 - Prioritize the most important opportunities in the field for future STRAP solicitations (“grand challenges”) within the umbrella STRAP structure
 - Establish criteria for evaluating pathway relevant STRAP concepts/applications
 - Recommend how existing NCI programs could be integrated, and whether new standing services infrastructure programs should be established to support STRAP projects
 - Facilitate outreach/education to investigator community regarding STRAP program
- The umbrella STRAP solicitation might help determine which Pathway subgroups may need assistance in developing complete STRAP concepts or connecting with their respective communities
- The external community should drive the need for these subgroups
- Biomarkers permeates through most of the Pathways and may be considered a priority for this reason

Prioritizing Candidate Projects

Issues Addressed

Selection of opportunities for funding through a new STRAP program requires a transparent, inclusive process for identifying those opportunities that are most appropriate for a focused development effort. Scientific quality is an essential criterion for such a process. However, early translational research must also be judged by the technical feasibility of the development

plan, the potential impact on a critical unmet clinical or public health need, and that the opportunity is unlikely to be addressed by industry.

Using the TRWG Developmental Pathways as a framework, various approaches for prioritizing candidate projects with the criteria listed above were presented to the NCI PATS Working Group. Questions posed included:

- What is the relative importance of the high-level criteria which includes
 - Significance of unmet clinical or public health need
 - Scientific validity
 - Feasibility of the development plan
 - Unlikely to be advanced by industry
- Which process best balances credibility, transparency and timeliness? Is timeliness more critical than transparency?
- Should different processes be used for different stages of prioritization (initial triage versus final selection)
- Should different prioritization processes be used for different Pathways?

Outcomes and Decision Points

NCI PATS Working Group members agreed that criteria for prioritizing STRAP candidate projects needed to be defined and clear, but had mixed viewpoints regarding the relative importance of the criteria. Many felt unmet clinical or public health need was a primary consideration, whereas others felt they were all equally important. The recommendation was to review applications under the umbrella STRAP solicitation using one or more Special Emphasis Panel like bodies but the process for defining the review criteria will need further discussion.

Points discussed with general agreement

- Ensure that we fund the best overall *project*
- Potential human benefit should be expected to occur in a reasonable time (i.e. within the timeframe of the STRAP award)
- Will need to consider how to prioritize between Pathways
- Need to develop a communication strategy for STRAP program prioritization and widely disseminate it

Funding Strategies

Issues Addressed

Due to time constraints, the NCI PATS Working Group did not have a formal discussion around funding strategies, however, a majority of the discussion items within funding strategies were referenced throughout the meeting. Potential funding models for consideration include funding an individual STRAP concept by integrating currently funded components whenever possible, creating a new standing infrastructure that provide key services that most STRAPs in a Pathway would require (similar to Agents Pathway and the NCI-funded NEXt program) or a hybrid model of some sort.

STRAP specific funding strategies are intended to:

- Fund a discrete and time-limited scope of activity
- Provide for active management and milestone-driven funding
- Provide additional resources for project management and leverage multiple mechanisms (grant, cooperative agreement, contract, competitive supplement, etc.)
- Potentially fund an entire STRAP for unusually important opportunities
- Allow flexibility for NCI to modify/replace STRAP components proposed by investigators

Points discussed with general agreement

- Existing NCI infrastructure programs may provide certain services but not all
- Funding should be committed for full development plan providing milestones are met
- If milestones are not met, funding is terminated
- Funding linked to a specific project not ongoing support of investigator or team
- Success will lead to hand off to Phase III trial, not renewal of funding
- NCI project managers to broadly facilitate and monitor project, identify needed resources and assist in problem solving
- Consider if NCI's The Cancer Genome Atlas program structure provides a useful model in whole or in part

Future Issues to Consider

The following issues were not actively addressed by the NCI PATS Working Group due to time constraints.

- Integration of review and funding processes for standing services infrastructure programs with review and funding of STRAP applications
- Expected number of STRAP awards and funding level associated with solicitation
- Will applications be reviewed by a single Special Emphasis Panel or a "parent" panel with sub-panels with expertise in technologies/pathways represented?
- If extramural experts are utilized for the concept review, can they be the same individuals that serve on the Special Emphasis Panel to review formal applications?
- If a solicitation focused on the Immune Response Modifier Pathway is to occur in the near future, would this Pathway be included in the umbrella STRAP solicitation?

NATIONAL CANCER INSTITUTE
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