**Toward a Fully Integrated Clinical Trials System**
Report of the Ad hoc Guidelines Harmonization Working Group
(Coordination Subcommittee, Clinical Trials and Translational Research Advisory Committee)
**July 2009** *(revised September 2009)*

## I. Introduction

The Clinical Trials Working Group (CTWG) of the National Cancer Institute's (NCI) National Cancer Advisory Board noted in its 2005 report that the productivity of the national cancer clinical trials enterprise will depend increasingly on collaborative team science. There are, however, structural factors that potentially hinder collaboration and a lack of incentives to develop a totally integrated clinical trials system. The structural factors are reflective of the many different elements through which NCI supports clinical/translational research, each of which are necessary but were developed independently over time within the Institute. Thus, guidelines for performance and for review of these organizational elements may not be aligned and may at times hinder integration and collaboration. It is also widely recognized that the current incentives within the NCI clinical trials system do not encourage cooperative efforts to efficiently develop new therapies for patients. The system will function more seamlessly in the future if NCI can develop language within its grant mechanism instructions and grant review procedures to promote collaboration across the spectrum of translational and clinical research mechanisms. The goal of this effort is to develop a fully integrated clinical research system whereby ideas generated by translational scientists working in SPOREs, P01s, etc. are moved through the early clinical trials process (Cancer Centers, U01 grants, N01 contracts) and into phase III trials coordinated by NCI-funded Cooperative Groups. In addition the NCI must assume a leadership position advocating for necessary academic, institutional, and professional cultural changes that recognize those who participate collaboratively in the enterprise as a whole and to remove barriers and disincentives to collaboration. Since this will be a long term effort, a special set of incentives must include provisions for the training and development of young investigators who will become the next generation of leaders in oncology.

### A. Background and Rationale

The CTWG envisioned that in a fully integrated clinical trials system, the Cooperative Groups, Cancer Centers, SPOREs, phase I U01 grants, phase II N01 contracts, and individual investigators will participate collaboratively in a joint enterprise guided by scientific priorities and informed by input from basic and translational scientists, community oncologists, and patient advocates. Sharing of data and ideas, and the development of true team science will become a new standard of excellence alongside individual and institutional achievement.

One of the CTWG recommendations was to "realign NCI funding, academic recognition, and other incentives to promote collaborative team science and clinical trial cooperation." A key element necessary to promote collaborative team science is to ensure that the guidelines for the different funding mechanisms supporting clinical trials are aligned. This should eliminate redundancy and duplication while proactively encouraging collaboration. The purpose of this document is to provide overall guidance and recommendations for the harmonization of NCI's clinical trials program guidelines

(Cancer Center, SPORE, Cooperative Groups, phase I U01s, phase II N01s, etc.) to achieve these aims. Other components of this initiative under active implementation are not described here; these include: 1) modification of NCI's clinical trials funding practices, 2) development of awards to recognize the contributions of clinical investigators, and 3) promotion of academic practices to better match the evolving needs of collaborative science.

These overarching goals were developed by members of the Guidelines Harmonization Working Group, part of the Coordination Subcommittee of the Clinical Trials and Translational Research Advisory Committee (CTAC) to identify areas that should be harmonized in the clinical trials program and reviewer guidelines to foster collaboration among the various components of the NCI-supported clinical trials infrastructure. The expectation is that NCI staff will review and modify the clinical trials program and reviewer guidelines to assure that they are congruent with the vision put forth in this document.

Finally, the members of the Working Group agreed that changes in guidelines for funding mechanisms will not, alone, provide incentives to overcome the structural and cultural barriers to collaboration across the spectrum of translational and clinical research. Therefore, this 'vision' document includes recommendations for consideration that go beyond revisions of guidelines.

## II. Approach

### A. Definition of Collaboration

Members of the Working Group agreed on the following definition of collaboration to guide their discussions:

*A method of working whereby individuals from different institutions and across NCI/NIH programs pool knowledge from relevant disciplines and share necessary resources to formulate and address clinical and translational research questions concerning cancer, pre-cancer or at risk populations. This approach allows investigators to more rapidly and efficiently reach knowledge-based conclusions than would otherwise be possible. The ideal collaborative structure facilitates recognition of individuals based on specific contributions, including the development and maintenance of core research resources, in addition to generation of new scientific knowledge.*

### B. Examples of Successful Collaborations

The members selected three examples of collaborations to illustrate the types of successful models of translational research and collaborative clinical trials that would be the intended outcome of implementation of the Working Group's recommendations.

**Development of Bortezimib/Velcade®** – a collaborative effort among industry, NCI, academic trialists, foundations, and patient advocates. Coordination among stakeholders facilitated validation of the discovery and preclinical development of the drug and reduced the time for enrollment of multiple myeloma patients into phase II trials and ultimately, FDA approval. Collaborative efforts were able to overcome common barriers to moving new drugs through the phases of development and validation.

**I-SPY Trial (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis) –** a collaboration among 7 sites, including five SPORES and two Cooperative Groups, as well as the NCI's Center for Bioinformatics. The collaborative partners established processes and principles for sharing of data and biological materials, standard protocols for quality control of biospecimens, MR imaging, and modification of procedures where necessary and appropriate to allow participation of partner institutions.

**SELECT Trial (Selenium and Vitamin E Cancer Prevention Trial)** – an example of a large, phase III study in which ancillary studies were incorporated, including nested observational studies on cancer or non-cancer disease areas, quality of life studies established as secondary endpoints, and correlative studies utilizing the biospecimen repository.

### C. Activities and roles of the major NCI-supported clinical trials programs reviewed by the Working Group

The Working Group focused its deliberations on the major mechanisms that the NCI utilizes to support clinical trials, as described below. Other mechanisms for clinical trials and infrastructure support were included in the discussions as elements of the clinical and translational research system, however specific guidelines were not proposed since these grants do not constitute "stand alone" programs, per se.

#### Cooperative Groups

The essential purpose of the NCI Clinical Trials Cooperative Groups is to support organizations that continually generate and conduct new clinical trials consistent with national priorities for cancer diagnosis and treatment research. The primary emphasis is placed on definitive, randomized phase III studies for cancer diagnosis and treatment and the developmental efforts preliminary to those trials. Cooperative Group studies address the delivery of concepts discovered and developed by Cancer Centers and SPOREs aimed at improving the diagnosis, prevention and treatment of cancer.

#### Specialized Program of Research Excellence (SPOREs)

The SPORE program was initiated by the NCI to promote interactions between basic and applied scientists for the development of new approaches to the prevention, early detection, diagnosis, and treatment of human cancer. The objective of the program is to encourage a diversity of approaches to translational research. Translational research in SPOREs is always based upon knowledge of human biology stemming from research involving the use of any cellular, molecular, structural, biochemical, genetic and/or other appropriate experimental approaches. SPOREs conduct early-stage interventions to establish the feasibility or proof-of-principle of specific approaches in cancer. Currently, all of these research projects whose goals are the development and testing of interventions are expected to reach the feasibility testing stage in humans within the anticipated 5-year periods of grant support. Similarly, studies that seek to determine the biological bases for observations in human cancer are expected to do so within 5 years. Bio-behavioral research projects that focus on links between biological variables, processes, and mechanisms pertaining to behavior and/or psychosocial variables are appropriate to include in SPORE programs.

SPOREs have seven common features: 1) Translational Research Focus, 2) Collaborative Design and Implementation of Research Projects, 3) Flexibility to Change Research Direction/Team Approach, 4) Specialized Research Infrastructure, 5)

Fostering Translational Research Careers, 6) Research Collaborations, Networks, and Consortia, and 7) Sharing Information, Data, and Resources.

**Cancer Centers**

NCI-designated Cancer Centers exhibit six essential characteristics: 1) Facilities dedicated to the conduct of cancer focused research, and to the center's shared resources, administration, and research dissemination, 2) Organizational capabilities for the conduct of research and the evaluation and planning of center activities, 3) Transdisciplinary collaboration and coordination, 4) Cancer focused research, 5) Institutional commitment, and 6) a Center director who is a highly qualified scientist and administrator.

The purpose of an NCI-designated Cancer Center is to take advantage of all of the institution's cancer research and research dissemination capabilities. An institution or consortium of institutions with meritorious programs in laboratory, clinical, and population research must integrate these into a single interdisciplinary and transdisciplinary Cancer Center research enterprise across departmental, school, and institutional boundaries. A Cancer Center should feature vigorous interactions across its research areas. These collaborations should facilitate rapid transfer of clinical observations to laboratory experiments, and promising discoveries in the laboratory to innovative behavioral and medical applications in prevention, detection, diagnosis, treatment, and survivorship. Cancer Centers are encouraged to collaborate and coordinate their clinical research efforts with other NCI-funded programs and investigators. These collaborations may include advancing research ideas from pilot studies to phase III trials (with transfer between various NCI-funded programs, where appropriate), providing correlative science services for large multi-site studies, and participating in multi-site trials conducted through the NCI-supported clinical trials systems. Cancer Centers are also expected to foster translation between the laboratory and the clinic, and to conduct early proof-of-principle, investigator-initiated clinical trials. Cancer Centers are encouraged to engage with industry in the development of scientifically promising studies involving new diagnostic tests, technologies, equipment, and therapeutic agents. Investigator-initiated trials are considered of significant importance in assessment of Cancer Center performance. Whereas phase I and early phase II trials supported by R01, U01 or N01 grants play a critical role in supporting such trials, it is not uncommon that pharmaceutical company or institutional funds are also used.

**Community Clinical Oncology Programs (CCOPs) and Minority-Based CCOPs (MB- CCOPS)**

The overall objectives of the CCOP and MB-CCOP programs are to develop and conduct state-of-the-art cancer prevention clinical trials, and diagnosis, control and treatment clinical trials with prominent involvement of community oncologists and engagement of the populations that they serve. For the MB-CCOPS there is an emphasis on minority patients in an effort to eliminate cancer health disparities. Overall, the CCOP network is designed to: 1) Increase the involvement of community oncologists and other specialists and their patients in clinical trials designed by NCI Cooperative Groups and Cancer Centers, 2) Involve a wider segment of the community in cancer clinical trials, and 3) Accelerate the transfer of knowledge gained from clinical trials to community oncology practices.

## D. Current Disincentives across Major Components of the NCI-Supported Clinical Trials System

Current disincentives and barriers to collaboration across clinical trials mechanisms were identified by review of current guidelines and through discussions of the Working Group. Disincentives to collaboration exist because of inconsistencies between guidelines, lack of specificity of guidelines for grantees and reviewers, or due to the organizational cultures and fiscal realities within components of the clinical trials system.

General observations:

- Limited reimbursement for patient accrual is one of the major disincentives to participation in Cooperative Group trials. The historical tendency to weight accrual to investigator-initiated trials more heavily in peer review of Cancer Centers has proven a disincentive as well.
- Cooperation among Cancer Centers is viewed as critical to the success of initiatives, but there is no incentive to use Cancer Center Support Grant (CCSG) resources to foster such activities. Subcontracts of collaborators do not count toward the NCI benchmark ratio, which is used to estimate approximate award level.
- SPORE applicants are asked to provide a plan to show how the SPORE will augment and/or complement any existing specimen resources supported by the CCSG or other mechanisms to avoid duplication, maximize productivity, and benefit from already-established infrastructure, including databases. On the other hand, within CCSGs, the primary users of shared resources tend to be Cancer Center investigators. Infrastructure control is often a powerful incentive to develop parallel resources such as data management and statistics, rather than shared cores.
- Collaboration on inter-SPORE and Cooperative Group trials varies between institutions, Cooperative Groups, and SPORE disease sites. Success is more a result of leadership influence rather than as a result of an integrated clinical trials system.
- Moving trials from phase I and II programs to phase III Cooperative Group trials often relies on program leaders within institutions who are also leaders in Cooperative Groups and can “champion” a particular trial. This limits the number of concepts that are likely to move across the translational/clinical spectrum at any one time.
- SPOREs frequently pursue the kinds of research questions that can only be studied through collaborations, networks, and consortia. These collaborative efforts are needed to develop the critical infrastructure needed to sustain translational research objectives for projects within the SPORE, as well as with other SPOREs and other research groups within the biomedical research community. Collaborations with existing NCI-supported clinical trial mechanisms have not been consistently encouraged as a means to promote rapid translation of promising laboratory discoveries to application.
- Recently updated Cooperative Group guidelines and review criteria instruct reviewers to give positive consideration for accrual to trials by Group members whether or not the trial is not being led or endorsed by the Group. However, there is the need to provide additional emphasis and incentivization for collaborative activities such that meaningful participation in these studies is considered to be as important as the scientific contribution the Group provides through development and accrual to its own studies. This includes cross-Group accrual to phase III studies and to selected phase II studies via the Cancer Trials Support Unit (CTSU) collaborative activities of the Groups, as well as with other NCI-funded programs and with investigators conducting clinical studies and trials (e.g., Cancer Centers, SPOREs, R01, and P01 investigators, etc.).

## III. RECOMMENDATIONS

**Summary:**
The Working Group proposes a two-pronged approach to developing collaborative clinical trials activities that will move the current clinical trials system to a seamless continuum of translation from basic studies to applications that benefit people.

A. **Revise Guidelines** for NCI clinical research support mechanisms to improve collaboration and ensure consistency across and between funding mechanisms. Instructions to reviewers must provide clear guidance for review and on how to give scoring credit for collaboration in the development and conduct of clinical trials.
B. **Develop Incentives to Collaboration:** The Working Group members agreed that guideline changes alone will not be sufficient to stimulate a collaborative culture. Therefore, the following proposals are included to provide additional incentives to move novel proposals across translational and clinical research programs.

    - Increase funding for PI and investigator time, including the expansion of U10 grants to qualifying institutions that participate in Cooperative Group trials.

    - Evaluate the effectiveness of the "Grand Opportunities (GO)" Grants for Coordination of Clinical/Translational Research across the NCI with the intent of developing a mechanism for long-term support using similar grants.

The recommendations described in this section are meant to be used by NCI Staff to develop specific revisions to guidelines for NCI clinical research support mechanisms, as well as plans for proposed incentives. NCI Staff are asked to provide a progress report to this Working Group and the CTAC within 6 months of acceptance of this report by the CTAC membership.

**Recommendations:**

**A. Guidelines**

1. **Guidelines for clinical research support mechanisms should require applicants to describe collaborative efforts across clinical trials and translational science mechanisms in a specified section of the application.** The section would be reviewed against certain discrete criteria and evaluated as an important element of the application, receiving an adjectival descriptor or rating in peer review. This section would highlight the importance of collaboration and consolidate in one section of the application, all of the examples that the PI wishes to illustrate, while standardizing expectations.

   Including collaboration as an essential characteristic for a Cancer Center or SPORE would be a further emphasis of the importance of collaboration.

2. **Applicant and reviewer guidelines should provide meaningful and specific guidance on what is needed to receive credit for active collaboration across the NCI translational and clinical trials system. This credit should be reflected in the overall priority score.** Such collaboration on studies that serve the overall goals of the NCI clinical trials system is to be considered positively in review. The Working Group members recommend the proposed guideline changes to consistently promote collaboration across all relevant funding mechanisms. These recommendations will be

addressed by NCI Staff in synchrony with other ongoing efforts to enhance the programmatic and review processes for clinical and translational trials.

3. **Incentivize trans-mechanism collaborations with the goal of facilitating transition of novel interventions from pre-clinical and early clinical development to definitive phase III trials.** Through greater involvement of SPOREs, P01s and Cancer Centers, prevention, diagnostic, or therapeutic interventions generated by these programs would be examined in definitive Phase III trials, thereby defining new standards of care developed through collaborations across the NCI clinical trials program.

    - Revise goal statements for all mechanisms to emphasize collaborations between components of the NCI clinical trials program that focus on pre-clinical and early clinical development of novel interventions including collaboration among Cancer Centers, SPOREs, P01s, and other funding mechanisms that offer access to novel clinical trials. The program guidelines for Cooperative Groups should also be modified to incentivize development of concepts for trials that have the potential to address specific scientific questions by broadening collaborations with other components of the NCI clinical trials program such as SPOREs. This approach would serve to maximize the scientific output generated by the core clinical trial through collaborations between SPORE and Cancer Center investigators.

    - A component of leadership review criteria for success as applied to the funding mechanisms evaluated by this working group should assess how well the leaders facilitate interactions across components of the clinical trials system.

    - There should be clear review criteria to guide reviewers in recognizing and providing credit for inter-SPORE, Cancer Center, and Cooperative Group collaborations, with increased weight for phase III trials for both treatment and prevention developed through collaborations of Cooperative Groups with Cancer Centers and SPOREs.

    - Cancer Centers and SPOREs should be encouraged to conduct and prioritize early phase treatment, diagnosis, and prevention clinical trials in collaboration with phase I U01 holders and phase II consortia and to partner with Cooperative Groups for conduct of late phase II and phase III trials. Similarly, the guidelines for the phase I U01 grants and phase II N01 contracts should be modified to strongly incentivize interactions with SPORES and Cooperative Groups. The Cooperative Group infrastructure for multi-site trials should be better utilized in those trials involving multiple sites. For example, new N01 contracts should be asked to include a plan for specifically interacting with SPOREs and Cooperative Groups.

    - Each SPORE should be encouraged to participate in trans-NCI mechanisms for phase II trials (treatment or prevention), utilizing the NCI's Cancer Trials Support Unit (CTSU) when possible to manage the trials, thus making the CTSU available to both SPORE disease-site and other investigators. Such trials could be reviewed and endorsed via the Disease-Specific Steering Committees. To be effective, the Disease-Specific Steering Committees will need to be authorized to review and prioritize such trials. SPORE sites that lead such trials should receive review credit and/or supplemental funding (if available) for this leadership effort. Similarly, any Group that mounts a phase III trial based upon a SPORE phase II trial with a SPORE co-PI should receive review credit and/or supplemental funding (if available) for this leadership effort.

- Cooperative Groups that mount a phase III study based upon early results from an NCI-funded Cancer Center study (i.e., SPORE, R01 or other R award, consortium, or P01) could receive supplemental funding for this trial. Additional review credit could be provided if the Cancer Center PI of the early trial is a co-PI of the phase III trial and/or the scientists whose work led to the trial are included as co-investigators. The intent is to provide opportunities for basic science investigators to remain engaged, particularly in the correlative science studies generated from the pre-clinical research that is performed in conjunction with phase III trials.

- Develop incentives to enhance greater collaboration between CCOPs/MB-CCOPs, Cancer Centers, and Cooperative Groups specifically to accelerate the transfer of knowledge gained from clinical trials to community oncology practice (T2-type translational research).

- Cancer Center guidelines should be revised to encourage (with increased funding credit) Cancer Centers to increase the NCI and other externally peer reviewed portion of their clinical trials portfolio.

- Support pilot projects and competitive supplements requiring multi-disciplinary and translational collaborations, e.g., between SPOREs, Cancer Centers, Cooperative Groups and the NCI-funded early clinical trials programs. Establish clear benchmarks for demonstrating that collaborative goals are being achieved.

**B. Incentives to Collaboration:** The Working Group proposes that in addition to updating guidelines across mechanisms, it will be critical to stimulate collaborations through efforts generated by specific investigators attempting to solve a problem. It is therefore proposed that in addition to the specific recommendations outlined below new mechanisms or expansion of existing mechanisms, if appropriate, be designed to move exciting, novel, clinically applicable ideas from bench to bedside through the clinical trials system - transcending cultural barriers and research silos. The members noted that in the current fiscal environment it will be important to couple any proposed new mechanisms with other initiatives such as the TRWG STRAP (Translational Research Working Group, Special Translation Research Acceleration Project) awards which are currently in the planning stages.

**1. Salary support and individual investigator recognition are considered to be important incentives to collaboration:**

- Salary support should be provided to institutional PIs through the Cooperative Group mechanism:
  - to oversee the Cooperative Group program within their institutions;
  - for the design and analysis of methods to improve quality and timeliness of protocol approvals; and
  - to support efforts to work across mechanisms to accrue patients to trials.
- Create a “Chair’s Fund” for Cooperative Group chairs to develop creative ways to collaborate across SPOREs and Cancer Centers.
- Increase the number and budget for U10 grants to qualifying institutions for participation in Cooperative Group trials.
- Guidelines should allow for support of PIs who collaborate across programs/mechanisms on common scientific questions and to enable access to technical resources and expertise, for example, SNP analysis, imaging technologies, molecular diagnostics and therapeutics, etc.

2. **Mechanisms are needed to enhance recognition and career development for individuals who make substantive contributions to collaborative clinical trials efforts, but are not currently Principal Investigators (PIs).**

    - Establish performance criteria and designations, such as "Scholar", "NCI Quality Investigator" to recognize contributions of individuals who serve on various clinical trials committees, study sections, etc. New forms of recognition for cancer clinical investigators were recommended by the CTWG and recently implemented with the specific proposal to create a new "Cancer Clinical Investigator Team Leadership Award" for mid-level clinical investigators not currently holding PI status on an NCI Grant.

    - Utilize current K-award mechanisms to tailor an award for senior investigators that would provide salary support, primarily for the facilitation of collaboration across institutional programs.

3. **Collaborative efforts to enhance patient accrual are considered to be key to successful cancer treatment and prevention clinical trials efforts.**
    - The Working Group members emphasize the critical importance of increasing per patient reimbursement, while recognizing that reimbursement issues must be addressed programmatically by the NCI.

    - Credit in review summary statements and overall priority scores should be given to individual Cooperative Groups, Cancer Centers, and other investigators for participation, both in scientific leadership and in accruing patients to peer-reviewed trials no matter who leads the trial.

    - Guidance to reviewers should include evaluation of whether the record of patient accrual to non-Group, non-endorsed CTSU studies is significant, along with a definition of "significant".

    - The capacity of the Cancer Trials Support Units (CTSUs) should be expanded, as necessary, to accommodate registration of patients for large Phase II trials originating from Cancer Centers and/or SPOREs. This would reduce or eliminate the need to establish and fund separate infrastructures for such trials and enhance accrual and collaboration.

4. **Formalize a process to facilitate development, review, support, initiation, and conduct of collaborative randomized phase II cancer treatment, diagnosis, and prevention clinical trial concepts.** Currently, most concepts for evaluation through the SSCs are submitted from one of the Clinical Trials Cooperative Groups. At times there may be a trial concept from an investigator or study team other than a Cooperative Group which is evaluated and recommended by the SSC. Non-Cooperative Group study teams are encouraged to collaborate with a Cooperative Group and access existing infrastructure for conducting multi-center clinical trials. There should be incentives, including the possibility of funding supplements, to support these collaborations, particularly when a proposed clinical trial would not be feasible or would be less meritorious without such collaboration. It is important to provide access to resources such as the Cancer Trials Support Unit (CTSU), data coordination, and/or standard accrual reimbursement to SSC-recommended collaborative Phase II trials.

5. **Evaluate the effectiveness of the "Grand Opportunities (GO)" Grants for Coordination of Clinical/Translational Research across NCI with the intent of**

**developing a mechanism for long-term support of similar grants.** The NCI recently released an RFA (RFA-OD-09-004) in conjunction with the American Recovery and Reinvestment Act (ARRA) program to support research on high impact ideas that lend themselves to short-term, non-renewable funding and may lay the foundation for new fields of investigation. The RFA is focused on furthering the high-priority goal of accelerating high impact translational research by encouraging and rewarding collaborative team science. It targets 2 years of support for team science by currently funded members of multiple research programs, including, but not limited to Cancer Centers, SPOREs, Cooperative Groups, P01s, R01s, or other NCI-supported translational research mechanisms. Evidence-based, hypothesis-driven correlative studies must be associated with either ongoing clinical trials or new (ready to proceed) clinical trials in multi-institutional settings. The Working Group members agreed that it will be valuable to build on this initial investment as a model to develop a new mechanism that will move exciting, novel, clinically applicable ideas from bench to bedside through the clinical trials system – transcending cultural barriers and research silos.

## IV. OUTCOMES MEASURES

The Clinical Trials Working Group established the need to include evaluation as an integral part of program management for both process and outcomes of implementation of CTWG recommendations. Additionally, they suggested outcomes measures that might be applied to such an evaluation. Consequently, a team of evaluation specialists proposed a set of measures which were used to initiate a baseline feasibility evaluation. Using these measures as a guide, the Guidelines Harmonization Working Group members propose that the following be used to measure the effectiveness of the recommendations, as implemented, in addressing the goals of the CTWG initiative to "*Realign NCI funding, academic recognition, and other incentives to promote collaborative team science and clinical trial cooperation."* Periodic reviews can be valuable to inform any future re-alignments to further enhance collaborative clinical trials.

Anticipated measurable outcomes of the recommendations of the Working Group, when implemented, include:

1. Guidelines for all NCI-supported clinical trials mechanisms promote collaboration with other clinical trials programs, e.g., Cancer Centers and Cooperative Groups.

2. Guidelines are consistent across mechanisms regarding collaborative activities in clinical trials.

3. Reviewer credit is reflected in overall priority scores for active collaborations across clinical trials and translational research programs and mechanisms.

4. Collaborative activities in early clinical interventions are demonstrated between Cancer Centers, SPOREs, P01s, and other programs that offer access to novel clinical interventions.

5. Cooperative Groups activate phase III trials based on results from early phase studies in other NCI-supported clinical trials programs.
    - The goal is to document a steady increase in SPORE/Cancer Center-generated late phase II and phase III clinical trials with an increasingly significant role of SPORE and Cancer Center scientific contributions to phase III Cooperative Group trials.

6. Incentives and rewards are instituted to promote early clinical research activities between Cancer Centers, SPOREs, P01s and other clinical research programs.

7. Performance criteria and rewards include individual contributions to collaboration on clinical trials.
    - The goal is to document increased contributions by SPORE and Cancer Center leadership to early phase NCI-sponsored trials and Cooperative Group late Phase II and phase III trials.

## V. Conclusions

The purpose of this document is to provide guidance to the NCI in the effort to develop a fully integrated clinical research system. The goal is to increase and facilitate the movement of ideas generated by translational scientists working in SPOREs, P01s, etc. through the early cancer treatment, diagnosis, and prevention clinical trials process (Cancer Centers, U01 grants, N01 contracts) and into Phase III trials coordinated by NCI-funded Cooperative Groups. Two major approaches to achieve this goal are proposed: (1) Revise guidelines for NCI clinical support mechanisms to improve collaboration and ensure consistency across and between funding mechanisms, and (2) Develop new incentives to stimulate collaboration. The Working Group members believe that implementation of these recommendations have the potential to play a critical role in fostering a collaborative, integrated clinical trials system.