Coalition of
CANCER COOPERATIVE GROUPS

Public Comment

Guiding Principles to Ensure Successful Reconfiguration of the Cancer Cooperative Groups

May 19, 2011

Statement of Need

On September 20, 2010, cooperative group chairs, through the Coalition of Cancer Cooperative Groups (Coalition), issued a public comment fully endorsing the Institute of Medicine (IOM) analysis "*A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program*" (April 2010). The statement urged that the IOM's recommendations be adopted *in their entirety*, and it voiced our willingness as the cooperative group leadership to work with the IOM, National Cancer Institute (NCI), advocacy organizations, and other stakeholders throughout the academic, governmental, and commercial sectors to develop *reasoned implementation plans* to transform the cooperative group program as recommended.

In this second public comment, we voice our consensus opinion on upcoming changes to the federal funding mechanism by which the cooperative groups will apply for multi-year grant awards from the NCI. The as-yet-to-be-written *Funding Opportunity Announcement* (FOA) will set forth new criteria by which the groups will be reviewed, ranked, judged, and funded in the future. It is expected that many of the IOM recommendations will coalesce in this FOA; thus, it carries the heavy weight of permanence in that it will set the groups' scientific and operational parameters over the long-term. However, simultaneous to the FOA development, several groups are in the midst of voluntary consolidations (IOM Recommendation #1) whose scientific and operational details are being defined. The irreversible forward momentum of these two parallel timelines has created a need for us to comment publicly.

The NCI has circulated a tentative timeframe for the FOA development, including a period for public comment through July 2011. After the period of public comment concludes, various internal NCI committees and the National Institutes of Health (NIH) will develop the FOA, which is scheduled for release in July 2012. We believe that during the period of public comment, it is imperative to clarify and define the components of a successful re-configuration of the cooperative groups. We have agreed upon a set of guiding principles to ensure that we ourselves advocate consistently for *reasoned implementation plans* to transform the cooperative group program as recommended. By making these principles publicly available, we trust that we are providing greater clarity for stakeholders during these final days of the public comment period.

The IOM report was the catalyst for various changes to the system that are now underway, and it has generated a new level of enthusiasm within the cooperative group leadership. Over the last several months, group leadership, working with the NCI, has made considerable progress in implementing many of the recommendations in the IOM report, such as increasing the efficiency of group operations, implementing a cross-group information technology (IT) system, and developing plans to consolidate the activities of certain groups into new relationships and entities. There are two over-arching principles on behalf of cancer patients in all of these activities: the first is to provide the framework for the groups to design and conduct innovative, science-driven clinical trials across the clinical research spectrum for the benefit of cancer patients--from advancements in treatment standards and improvements in quality of life to cutting edge early detection, prevention, and diagnostic capabilities. The second principle was well articulated in the IOM report, that "it is imperative to preserve and strengthen unique capabilities of the cooperative group program as a vital component in the NCI's translational research continuum."

Guiding Principles to Ensure Successful Reconfiguration of the Cancer Cooperative Groups:

1. **Patients are best served by having strong scientific programs**
2. **The cooperative groups will function as an integrated hub for large Phase II and Phase III studies**
3. **Flexibility is required to maximize the potential of the restructured system**
4. **The strong membership culture of the groups is worth preserving**
5. **The study review process should incentivize scientific innovation**
6. **The viability of the new cooperative group hub is linked to its critical resource needs**
7. **Multi-sector involvement generates funding and science that would not otherwise happen**
8. **Applicants for cooperative group funding should possess certain *Essential Characteristics***

Principle #1: Patients are best served by having strong scientific programs

The cooperative groups are, at their core, multi-disciplinary, multi-institutional, and multi-disease oriented science-driven clinical research organizations which perform clinical trials designed to move the standard of care forward. The re-configuration should enhance the ability of the groups to perform innovative, science-driven clinical trials. To do so, the new review funding criteria for the groups should give the greatest consideration to each group's scientific expertise, followed by what it brings to the network as a whole. This will help ensure that the groups remain focused on improving the outcomes for patients with cancer.

- The new review criteria should judge the groups upon their ability to design and perform science-based large Phase II and Phase III studies that complement and balance the more tailored approach of industry toward FDA primary and secondary filings for drug approval, e.g. evaluating new targeted agents across disease types not encompassed in the initial FDA filings; determining the optimum characteristics for patient selections across disease types based upon their molecular and genetic characteristics, and designing trials in selected subsets of patients based upon those characteristics; direct comparisons of competing new therapies or combinations of therapies, some of which may be held by more than one company, or may be non-pharmaceutical therapies; and quality of life research.

- In order to perform such studies, the groups must have ready access to agents in development. It is important to acknowledge that while the groups will be judged for their science, and for what they bring to the newly integrated network, it is the role of the NCI to provide ready access to agents within its portfolio.

- A major reflection of the quality of science being performed in the groups is their ability to call upon the specific strengths of their membership to produce NCI funding via R01s, P01s, SPORES, contracts, and other publicly and privately funded peer review mechanisms. The new review criteria should stimulate scientific innovation to flow more efficiently from the cancer centers to the cooperative groups by coordinating leadership and prioritizing cancer centers' biomarker-based research, genomics, novel study designs, and promising Phase II studies**.**

- The system is best served by continuing to have independent, academically-based statistical leadership integrated into each group's scientific leadership.

- Annotated biospecimens, and the biorepositories that process and hold them, are essential to science-based studies. There are three needs in this area: 1) to maintain the current practice of integrating them into group operational/scientific structures; 2) to provide the IT infrastructure to link biorepositories together *aka* a virtual biorepository; and 3) to develop a more robust system to provide to biospecimens for peer-reviewed research.

Principle #2: The cooperative groups will function as an integrated hub for large Phase II and Phase III studies

Cooperative groups are connected by their cross-group scientific and administrative interactions. While each possesses unique capabilities, the cooperative groups are best viewed collectively, within the newly integrated network, as the hub for Phase II and Phase III studies. The NCI should clearly declare that the re-configured cooperative group system is its major vehicle for performing large Phase II and Phase III studies within its translational research continuum.

- Together, we are committed to developing, performing, and providing the logistical and infrastructure support for large Phase II and Phase III studies independent of which group originates the study. As a corollary, the new criteria should reward network participation by giving equal credit for all trials in which a group and its' members participate.

- We are committed to developing a governance structure to manage cross-group scientific and administrative functions, in conjunction with the NCI, which will include developing guidelines for interactions between the group scientific structure and the steering committees, aligning scientific priorities, creating consensus, and enforcing decisions made by the network leadership.

- Together, the groups are working with the NCI on an integrated IT infrastructure to support studies performed within the network, including the development of a "virtual biorepository" to facilitate access to biospecimens.

- The groups are working with the NCI to continually improve operational efficiencies.

Principle #3: Flexibility is required to maximize the potential of the restructured system

The cooperative groups are in the process of restructuring, and once consolidations are complete, the groups will look different from one another based upon their need to preserve and enhance areas of scientific and functional expertise. It is likely that some groups will remain as currently structured, some will combine into one entity, and some into a confederation alliance of several entities. The new federal guidelines for grant review should allow groups to make their own decisions about the formation of their structures—scientifically and operationally.

- Flexibility is needed to preserve and enhance areas of scientific expertise within the groups, e.g. one group may relate more successfully to patients, physicians, researchers, and other people working in a particular disease specialty, or it may be the groups need to form an imaging hub or laboratory to be available for the entire network; flexibility will be required for the groups to determine how such capabilities fit into the entire system.

- The new federal funding guidelines should not require excessive homogeneity in the cooperative groups, or in other words, the criteria should not require groups to be too similar in structure, purpose, or capabilities. Otherwise, if every one of the groups looks the same, there will only be a general competition for funding rather than the more optimal mixing and matching of different scientific and functional expertise in the various groups.

Principle #4: The strong membership culture of the groups is worth preserving

The cooperative groups are member driven networks, which engender a culture of team science, commitment and volunteerism across three core areas of membership: cancer centers and academic sites; Community Cancer Oncology Programs (CCOPs), Minority-Based CCOPs and other community based practices; and patient advocates involved in research. The new review criteria should reward their strong membership culture as follows:

***Cancer Centers and Academic Programs*: the NCI-designated cancer centers, their clinical investigators, and laboratory programs provide the scientific engine that drives the development and design of Phase II and III studies within the cooperative group system. The reconfigured system should amplify these interactions.**

- Under the existing structure, the groups and the cancer centers have benefited mutually from their scientific interactions, e.g. during the last five years 66 RO1s, 6 P01s and 19 SPOREs relating to group work have been awarded to cancer center investigators.

- The entire NCI clinical research infrastructure including the cancer centers, R01 and related grants, SPOREs, Program Projects, and the reconfigured cooperative group system must be aligned accordingly to maximize the functional interactions among these programs. We endorse the recommendations of the Ad Hoc Guidelines Harmonization Working Group as presented to the Clinical Trials and Translational Research Advisory Committee (CTAC), and support their earliest possible implementation.[1]

- The U10 grant mechanism currently provides an integral connection between the scientific programs of the cooperative groups, cancer centers, and academic institutions; the number of U10 grants in the program should be increased so that additional qualifying institutions can connect to the groups.

- U10 Principal Investigators and individuals with senior leadership positions within the cooperative groups should be recognized in the senior leadership structure of the cancer centers, and the science they perform within the groups should be acknowledged and rewarded in the cancer center review process. The cancer center core grants should add metrics of success and impact for cooperative group participation via senior leadership positions and participation in active committee membership positions.

- In order to increase opportunities for young investigators to develop and lead clinical trials in the groups, we recommend that both the cancer center core grants and cooperative grant mechanism add aligned metrics of success and impact in the area of "career development."

***Community-Based Researchers*: CCOPs, Minority-Based CCOPs (MBCCOPs), and community practices affiliated with the cooperative groups are an integral component of the existing system and account for over half of the accrual onto group studies. Community-based researchers view the cooperative group structure as their scientific "home" where they can participate at all levels. They are best served by a cooperative group structure that is multi-disciplinary, multi-institutional and multi-disease oriented. The new review criteria should preserve and strengthen their membership ties with the groups.**

- The current structure provides the opportunity for CCOPs and MBCCOPs to align primarily with one cooperative group, but also allows them to participate in the activities of groups of their choosing through the Expanded Participation Project; this practice should continue.

- To provide a stable funding base, high accruing community practices should be provided the opportunity to receive increased per-case reimbursement and infrastructure support through an expanded U10 mechanism, or other such federally funded mechanisms. This is not currently the practice.

- The groups should continue to support, through the CCOP mechanism, risk assessment, early detection, prevention, symptom intervention, health outcomes, and special populations research.

[1] "Toward a Fully Integrated Clinical Trials System," July 2009. http://deainfo.nci.nih.gov/advisory/ctac/workgroup/GHWG%20Report_Rev.9-2009_FINAL.pdf. Progress reports to CTAC, December 2010. http://deainfo.nci.nih.gov/advisory/ctac/workgroup/GHWGimplementationReport.pdf, and http://deainfo.nci.nih.gov/advisory/ctac/1210/presentations/GHWG.pdf

***Cooperative Group Patient Advocates*: Approximately 100 individuals serve voluntarily as patient advocates in research across the groups; in each, advocates are involved in all aspects of study development, execution, and trial monitoring. The reconfigured cooperative group system must maintain the integral function of patient advocates in its scientific structure.**

- We recommend that the consolidation of some of the groups should not result in a substantial reduction in the number of advocates who participate in the groups.

- The high level of involvement of the advocates in all phases of trial development and execution should be maintained.

- In the newly configured system, patient advocates who participate in disease steering committees, SPORES and other parts of the integrated network, would benefit from having increased access to, and interaction with, the cooperative group advocates. Currently, functional interactions among the cooperative group advocates occur primarily through a structured program within the Coalition of Cancer Cooperative Groups.

Principle #5: The study review process should incentivize scientific innovation

In the area of scientific proposal review, we agree that extramural peer review facilitated by the NCI should be employed in assessing scientific proposals, and in helping to define the strategic landscape for a given malignancy. The steering committee approach is in varying stages of development and implementation across diseases; this approach should be evaluated primarily for its ability to encourage and incentivize scientific innovation. The entire concept of task forces should be reconsidered. We are developing a white paper discussing the Steering Committee process and its optimization. Listed here are some top line recommendations:

- Steering committees should be charged with reviewing studies, not designing or re-designing them, and the role of the NCI should be facilitative, rather than controlling, in the process.

- The entire process should be open and transparent.

- Unnecessary layers of review should be eliminated, particularly regarding establishment of multiple task forces.

- As noted in Principle 2, in conjunction with the NCI, we are committed to developing a governance structure to manage cross-group scientific and administrative functions. One imperative of the governance structure will be to develop guidelines for interactions with steering committees, particularly those needed to stimulate innovative trial approaches using disease specific markers and novel study designs.

Principle #6: The viability of the new cooperative group hub is linked to its critical resource needs

While it is widely known, accepted, and acknowledged by the IOM report that the cooperative group system is grossly underfunded, we also recognize the enormous economic challenges that face our nation. Unfortunately, the crisis in the economy occurs at a time when we are all committed to re-thinking how we operate and work together to enhance the opportunities for patients to participate in innovative ground-breaking clinical trials. As funding priorities within the NCI, NIH, and the federal government are assessed; it is still important to define the critical needs:

- Per Case Reimbursement. Recently, the NCI adjusted the base level funding for large Phase II studies to $5,000/case. The case reimbursement structure for Phase III studies must be addressed in the new federal funding opportunity; the base level funding of $2,000/case has become so non-competitive that it endangers the entire national clinical trials system regardless of its configuration. Current per case reimbursement for Phase III studies does not come close to covering the costs of participation in cooperative group trials. This places a burden upon institutions that participate in cooperative group studies to make up the difference through cost-sharing and dedicated staff members who donate their time—an unsustainable reliance upon volunteerism considering the rising cost of medicine. The case-reimbursement floor for Phase III studies should increase to $4,000, with additional reimbursement set trial-by-trial based on complexity and priority. Whatever the reimbursement for a given trial, the funding level should be the same for high accruing sites, whether they are academically or community based.

- Number of U10 Grants. The U10 grant mechanism currently provides an integral connection between the scientific programs of the cooperative groups, cancer centers, and academic institutions; an increase in the number of U10 grants in the program will enable additional qualifying institutions and their researchers currently "outside the system" to become members of the groups.

- Investigator Compensation. The U10 grant funding should increase, above and beyond case reimbursement, to adequately support investigators for their scientific participation in the groups.

- Common IT Platform. We appreciate the NCI's recent commitment of funds to a cross-group IT platform. Funding is needed for continued development and implementation of the uniform IT infrastructure, which includes protocol authoring, clinical trials data management, and biospecimen management.

- Biorepositories. Funding is required to fully support the groups' biorepositories. Three needs described in Principle #1 are restated here: 1) to maintain the current practice of integrating the banks into group operational and scientific structures; 2) to provide the IT infrastructure to link biorepositories together *aka* a virtual biorepository; and 3) to develop a more robust system to provide to biospecimens for peer-reviewed research.

Principle #7: Multi-sector involvement generates funding and science that would not otherwise happen

The groups bring significant incremental resources to the publicly funded system. Aside from the increased levels of funding defined above, the federal guidelines must continue to provide the flexibility for the cooperative groups to seek and maintain multi-sector funding relationships. These relationships provide a critical financial supplement to the federal funding, in support of NCI-approved clinical and laboratory based studies.

- Close working relationships with industry yield additional resources, on a trial-by-trial basis, to increase inadequate case reimbursement, support laboratory based integral and integrated biomarker studies, and/or address exploratory laboratory investigations. In the latter example, supplemental funding has led to more precise definition of disease and a better understanding of basic tumor biology.

- In addition to industry, the groups successfully generate funds from the non-profit sector, in support of NCI-approved studies relating to specific diseases, supportive care, and survivorship.

- The peer review system should reward groups for generating science through their foundations and bringing it to the network.

<u>Principle #8</u>: Applicants for cooperative group funding should possess certain *Essential Characteristics*

The purpose of the new federal funding guidelines should be to produce excellence in science and ensure groups remain focused on improving the outcomes for patients with cancer. To do so, we recommend that applicants to the upcoming funding opportunity possess the following *Essential Characteristics*:

1. Strong scientific base with representation from cancer centers, academic institutions, and community-based programs, including the Cancer Community Oncology Program (CCOP) and Minority-Based CCOP members;
2. Established track record in designing and executing clinical trials that move the science and standard of cancer care forward and/or change clinical practice;
3. Documented history of accruing large numbers of patients to high quality clinical research trials;
4. Strong, integrated, and established biorepositories and IT systems;
5. Proven track record in producing NCI RO1, PO1, and SPORE grants and contracts;
6. Capability to perform clinical trials that incorporate integral and integrated biomarkers, including imaging;
7. Operations/headquarters offices capable of conducting multi-institutional federally funded trials;
8. Academically-based statistical support and data management centers with a successful history of developing, monitoring, and analyzing multi-institutional Phase I-III clinical trials;
9. Robust and established membership structure that brings together both academic and clinically based experts into a multi-disciplinary, multi-disease, and multi-institutional structure; and
10. Track record in abiding by the timelines and guidelines of the NCI Operational Efficiency Working Group.

Signed,

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The Coalition of Cancer Cooperative Groups is an independent non-profit organization working to improve physician and patient access to cancer clinical trials through education, outreach and advocacy. For more information, visit www.CancerTrialsHelp.org or contact Diane D. Colaizzi, MA, Executive Advisor and Media Relations Liaison, 215.789.3612 and dcolaizzi@cancertrialshelp.org.