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Cooperative Group System Needs Change In Funding, Review Process, Report Says

The cancer clinical trials cooperative groups are in jeopardy, and changes are needed to enable the system to survive, chairmen of the groups wrote in a paper submitted recently to NCI Director Andrew von Eschenbach.

"Although the groups are recognized as the worldwide model for clinical research, the system faces numerous challenges that jeopardize its future," the groups said in a "white paper" presented to von Eschenbach at a closed meeting March 17.

The proposal, which was developed by the Coalition of National Cancer Cooperative Groups, recommends 25 ways to improve the publicly funded

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In Brief:

New AACR President Matrisian Plans 2004 Emphasis on Enhancing Communication

ORLANDO—**LYNN MATRISIAN,** the Ingram Distinguished Professor of Cancer Research and professor and chairman of the Department of Cancer Biology at Vanderbilt University, began her term as president of the American Association for Cancer Research at the organization's annual meeting here earlier this week. Matrisian said AACR plans to enhance its communication activities this year. "What I see AACR able to do is serve as a clearinghouse for information from its diverse membership," Matrisian said after succeeding **Karen Antman** as president on March 29. "We can do this by taking a scientific leadership role, synthesizing and disseminating information to enhance cross-disciplinary scientific communication." AACR plans to begin publication of an annual meeting report, an annual report on progress in cancer research, and highlights of its journal Cancer Research. Also, AACR plans to increase its staff from 102 to 120 this year, and hire a policy advisor to be based in Washington, D.C., to promote the organization's goal to "make cancer a national priority." . . . **PETER JONES**, the H. Leslie and Elaine S. Hoffman Cancer Research Chair at the University of Southern California, began his term as AACR president-elect. Jones is director of the University of Southern California/Norris Comprehensive Cancer Center; director of the Urological Research Laboratories and distinguished professor of biochemistry and molecular biology and urology at the Keck School of Medicine. **Karen Antman**, who is scheduled to officially begin duties as NCI deputy director for translational and clinical sciences on April 18, became past president of AACR. Prior to her appointment at NCI, she was the Wu Professor of Medicine and Pharmacology at the Columbia College

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Groups Recommend Change To Incentives, Review Process

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cancer clinical research system.

"A common theme of the recommendations involves correcting misalignments in the incentives, review processes and review criteria so that they support, not undermine, the mission of the system," the report states. "Each recommendation is important; cumulatively, they have the potential to create breakthrough improvement in the performance of the system."

While the groups want greater funding and greater autonomy from NCI, the Institute director appears to be pursuing a different agenda.

At a time when growth of appropriations for cancer research is slowing down, von Eschenbach is trying to carve out funds to pay for various initiatives, which include the National Biospecimen Network, a centralized tissue bank that may compete with the groups' tissue repositories. Another von Eschenbach initiative, the Cancer Biomedical Informatics Grid, or caBIG, is based in cancer centers, bypassing the groups (**The Cancer Letter**, March 12).

The white paper establishes a benchmark for comparison of the request from the groups with the outcome of an NCI-organized committee of advisors who are reviewing all clinical trials programs sponsored by the Institute.

"I know that some people may doubt this, but phase III trials are going to be required to define the activity of new treatments, molecular treatments and targeted treatments, any kind of treatments for the foreseeable future," said Robert Comis, chairman of Eastern Cooperative Oncology Group and chairman and president of the coalition. "So, if the government wants to maintain a responsible role in cancer research, the phase III system has to be enriched and nourished."

Last July, von Eschenbach called for a comprehensive review of the clinical trial systems (**The Cancer Letter**, July 11, 2003). Instead of resisting change, the groups offered a proposal that addresses the structural issues not only in the cooperative groups, but also in the whole system.

"We wanted to take a responsible role to work on our end on how we think not only the groups, but the whole system could be improved," Comis said. Leadership of the groups has met twice with von Eschenbach to discuss the change.

At the first meeting, in October, representatives of the coalition informed the NCI director that they planned to put together a white paper. At a subsequent meeting March 17, the coalition leadership presented the document to von Eschenbach.

"He was very well prepared, he was very engaged, and once again reaffirmed his commitment to cooperative groups, and the need to integrate the whole structure better," Comis said.

The structure of the NCI extramural programs should be changed, Comis said. "NCI is organized into silos," he said. "As a result, the extramural program is organized into silos. So there is no real reward or additional funding, or even additional recognition in the system for cooperation across the system. It's a perverse system right now, where you don't really get rewarded for cooperation."

The system should reward cooperation between cooperative groups, cancer centers, and SPOREs, Comis said. "One of our recommendations is that centers and SPOREs, which are heavily involved in early phase I and phase II trials, and we, who are involved in later phase II and phase III, should be integrated," he said. "There should be rewards for taking ideas from phase I all the way to the cooperative group system in phase III."

The Institute's caBIG program should include the groups, Comis said. "We want to be a part of the CaBIG program," he said. "Right now, it's oriented toward the cancer centers, but here you have the cooperative group system, where we have our biostatistical data management centers that manage 25,000 patients on therapeutic trials a year, and about 150,000 patients in

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Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: news@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
E-mail: info@cancerletter.com

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follow-up, all of which have carefully annotated tissue associated with it, so if you really wanted to integrate the best annotated data into the system, we need to be involved in this right from the start.

"The original thought was to go stepwise, with the centers first, but I think we need to figure out how to get involved in that now."

The groups have been hampered by NCI regulations and insufficient funding, Comis said. "We put more patients on clinical trials than any other system in the world," he said. "You can't run a system like that that's funded at half of what the peer reviewers approve us to be funded at and half of what it costs to do the work in the field."

The white paper suggests that the groups improve coordination of their activities. "To a great extent, the intergroup system and process have become dysfunctional," Comis said. "The group chairs, who ultimately have control of the resources, have been out of that loop."

The report recommends that the coalition should be the coordinating body for the intergroup process.

At the March 17 meeting, von Eschenbach agreed to put together a formal response to the white paper, said Richard Schilsky, chairman of the Cancer and Leukemia Group B and vice chairman of the coalition. "Dr. von Eschenbach agreed to meet with us within three months to review the NCI response," Schilsky said.

The NCI committee reviewing the clinical trials programs is expected to hold its first meeting sometime in May, sources said.

The text of the document follows:

The cooperative groups have played a key role in the Nation's cancer clinical research system for almost half a century. The groups, whose members include NCI-designated cancer centers, SPOREs, an extensive community-based provider network, and strong patient advocate programs have advanced the standards of care in cancer to save lives and to improve the quality of life of cancer patients.

The groups' pioneering work on adjuvant therapies, combined modality therapies, chemoprevention of cancer, and organ preservation has enabled countless cancer patients to become cancer survivors.

Although the groups are recognized as the worldwide model for clinical research, the system faces numerous challenges that jeopardize its future.

This proposal addresses the major challenges that hinder the cancer clinical research system and sets forth recommendations in five strategic areas:

1) Streamlining the clinical research structure and improving the working of its component parts;

2) Adapting the system to the development requirements of modern cancer therapies;

3) Establishing scientific priorities;

4) Accelerating protocol development; and,

5) Improving funding.

Mission and Background

The mission of the cooperative groups is to save the lives of cancer patients and advance the standards of care for cancer patients through publicly-supported clinical trials and correlative studies that are definitive, controlled, investigator-initiated, multi-center, and peer-reviewed.

As the only public alternative to industry, cooperative groups optimize the discovery, development, and delivery of new cancer screening, diagnostic, and therapeutic approaches, as the results of their studies are integrated into standard practice.

The groups and their affiliated community members conduct definitive multi-center phase III trials that assess novel therapeutic interventions and validate surrogate end points and hypotheses that are generated by the academic oncology community, including cancer centers and SPOREs, all of which are affiliated or participate with the cooperative groups.

Throughout their history, the groups have been an indispensable resource in the discovery, development, and delivery continuum that produces new cancer treatment and prevention strategies. By involving community doctors in their trials, the groups have become the engine for advancing the standards of care in a real-world setting, establishing what should be delivered. Their track record in reducing the burden of cancer is unmatched.

Major clinical accomplishments include:

•Demonstrating the benefits of adjuvant therapy in colon, lung, prostate, breast, ovarian, and cervical cancer;

•Developing combined modality therapies for solid tumors;

•Substantiating the use of chemoprevention in cancer;

•Developing curative therapies and dramatically increasing long-term survival rates in childhood and adolescent cancer patients.

For example, the National Surgical Adjuvant Breast and Bowel Project's Breast Cancer Prevention Trial results established the proof of principle that the incidence of breast cancer can be reduced, which led the FDA to approve the use of tamoxifen to reduce the risk of breast cancer in women at increased risk for the disease, the first such approval.

Since the BCPT results were first reported, other large cancer prevention trials have shown positive results in breast, colon, and prostate cancer (for example, the prostate cancer prevention trial comparing finasteride with placebo).

Additional prevention and early detection trials have been initiated and are well underway, setting the stage for further advances, much like the process that occurred 25 years ago with the first adjuvant therapy trials in breast cancer.

The vast majority of group trials include correlative studies performed in laboratories throughout the country.

The groups' high-quality laboratory studies have yielded a rich harvest of important results.

Some examples include demonstrating the relationship between Her-2/neu expression and anthracycline responsiveness in breast cancer, confirming 18q/MSI as a marker of colon cancer prognosis, developing risk-adapted therapies for leukemia, and showing the predictive value of EGFR overexpression in head and neck cancer patients.

The NCI clinical trials structure epitomizes the types of integrated research teams recommended in the NIH Roadmap initiative, and should be the model for future efforts. The groups manage more than 100,000 patients annually on high-quality clinical trials – therapeutic, prevention, translational, symptom-control, early-detection, and diagnostic.

Of those 100,000 patients, approximately 25,000 are enrolled annually on therapeutic trials, representing one half of all patients on therapeutic trials in the country. The groups provide access to broad patient populations for large-scale randomized trials, and have spearheaded minority-access, community-based programs, and studies of special populations.

The groups have also woven patient advocate participation into their organizations on a national scale, providing them with a unique platform to optimize the design of clinical trials and a voice to recommend improvements to the clinical research system.

Despite its singular role and contributions, the system faces chronic and harmful issues that threaten its ability to fulfill its mission.

The Armitage committee and implementation committee reports acknowledged many such issues during the late-1990s. In September 2002, the NCI Director's Consumer Liaison Group (DCLG) and the Coalition's Patient Advisory Board (PAB) produced a report evaluating the pilot programs that were created as a result of the Armitage committee report and the recommendations of the implementation committee.

A major conclusion of the DCLG/PAB report is that the challenges plaguing the system persist, and, in some cases, have worsened. For example, activating a trial has become a longer and more complex process, with additional review layers.

Funding levels continue flat and remain insufficient to cover costs. The autonomy of individual investigators, the driving force for innovation in the groups, appears constrained as the scientific agenda is controlled, rather than facilitated, by NCI. And, core laboratories and informatics enhancements continue to be inadequately resourced.

One result is that the system's most important professional constituency, clinical researchers, is questioning the value of continuing to participate in group studies. For current and future patients, the lengthy time to trial activation means that many will not receive treatment that could represent their best hope for survival.

Recommendations

The group chairs are committed to invigorating the system, making it more attractive to researchers and more vital as a force in helping to advance the standards of care in cancer.

In their deliberations during the past year, the group chairs have developed recommendations that they believe will animate the system and give it renewed vigor to achieve its mission. The remainder of this proposal articulates these recommendations, and classifies them by the five strategic goals listed in the introduction.

The group chairs are confident that, with the support of the NCI to help implement the recommendations, the time to trial activation will be significantly reduced and that the number of completed, high-quality trials will increase. In the process, the value of the system to patients and investigators will continue to grow as the important hypotheses in cancer prevention, early detection, and treatment are validated.

1. Streamlining the Clinical Research Structure. The cooperative groups, which include NCI-designated cancer centers, SPOREs, CCOPs, and other academically affiliated practices are an integral part of the nation's cancer clinical research system.

Every cancer center is a participant in at least one cooperative group, and cooperative groups serve as research bases for the CCOPs. Cancer centers holding SPOREs are also members of the cooperative groups. In all, more than 1,500 institutions throughout the U.S. and Canada, and approximately 8,000 investigators in these institutions participate in cooperative group trials.

The components complement each other: As centers and SPOREs drive the early stages of the discovery and development processes, the groups and CCOPs primarily fulfill the latter stages of the development and beginning stages of the delivery end of the process.

Unfortunately, the components of the system tend to function as a collection of disparate programs, as opposed to one integrated public system. The group chairs believe that the guidelines governing the centers, SPOREs, and groups should be harmonized to engender more cooperation and data-sharing (including, tissue and images) among the major programs.

For example, because standards of care cannot be advanced without phase III trials, the group chairs recommend that the performance of SPOREs and centers should be measured, in part, by the number of agents, ideas, or approaches that move into phase II and phase III cooperative group trials.

Similarly, the peer-review criteria should be modified to eliminate disincentives to cooperation and to encourage and reward collaboration. Financially, centers and SPOREs should receive incremental funding if they participate in group trials, for instance, when they serve as reference laboratories or provide bioinformatics expertise.

There should be no unfunded mandates or disincentives to achieve participation across the entire system. Patient advocates, who are involved in the review of each program's guidelines, should be included in the harmonization effort.

Another powerful way to improve collaboration is to eliminate restrictions on the mobility of investigators. Today, the unit of membership in most of the adult groups is the institution, not the individual. Consequently, investigators are tied to their institutions, which means that the system cannot readily access the best minds for science and leadership positions.

The group chairs propose to remove the barriers to improving the system, in part, by providing investigators access to the system's facilities, regardless of institutional affiliation.

The existence of separate groups enriches the scientific platform, because it permits each group to develop areas of special expertise. At the same time, a decentralized structure can lead to replication of functions such as administration and operations across the system.

A starting point in generating cross-group efficiencies would be to explore the consolidation or centralization of some of these functions. Before embarking on such a course, however, the group chairs recommend that the lessons of the merger of the pediatric groups into the Children's Oncology Group (COG) be fully evaluated.

Although the merger has been successful, it was more difficult and time-consuming than anticipated. Furthermore, operational speed and efficiency were initially sacrificed, because insufficient resources were made available to support the merger process, while work on nearly 100 active clinical trials continued.

Similarly, the group chairs recommend that, before any further centralization or consolidation efforts occur, the experience and track record of the CTSU be documented to determine how centralization of group functions through the CTSU has taken place, how the system has been affected (including costs and benefits), and how the strategies should change.

Since its first patient was enrolled in November 2000, the CTSU has accrued approximately 3,000 patients in total. Its current monthly accrual rate is 250 patients, for an annualized rate of 3,000 cases, representing 12% of the approximately 25,000 patients that the system accrues annually for therapeutic trials.

Because it has not been effective at general enrollment, the group chairs recommend that, in the area of patient recruitment, the CTSU should phase out its activities in general enrollment and focus, instead, on serving as the national enrollment catalyst for rare diseases, minority and underserved populations, and trials of drugs whose patent protection has expired.

While the other recommendations in this proposal are being implemented, the group Chairs propose to undertake a comprehensive six to nine-month study to identify more efficient organizational structures, workflows, and common data platforms to facilitate data acquisition and sharing across the groups, including the CTSU.

As part of the analysis, the group chairs will also evaluate the best ways to continue working with patient advocates to develop studies that are relevant and feasible, improve access to trials for minority and special populations such as the elderly, and accelerate the adoption of new standards of care.

2. Adapting the System to the Development of Modern Cancer Therapies. Phase III clinical trials will continue to be required to establish the efficacy of new cancer therapies in the age of molecular targets. These studies will need more carefully selected patient populations and more precise molecular definitions of the disease state, stage, and risk.

The groups are positioned to adapt to the development and delivery of targeted therapies, because they have the phase III capabilities and networks to recruit homogeneous populations on a national basis. The groups also have tissue banks with well-annotated clinical data linked to image archives, which are an integral part of the groups' science.

However, the groups need better access to core facilities, such as central molecular pathology and reference laboratories, to conduct rapid screening to identify appropriate populations for studies of targeted agents and to assess pharmacodynamic endpoints. SPOREs and centers, which could provide such core facilities to the groups, need financial incentives to support these activities.

Consequently, the groups and centers require stable funding to develop fresh tissue networks, pay for gene arrays, and fully conduct molecular profiling.

Investigators need access to an inventory of available reference laboratories and their capabilities. One simple way to do this would be for centers and SPOREs to list their laboratories on an NCI Website that would be accessible to cooperative group investigators and administrators. Thereafter, work could begin to standardize the operating procedures across the laboratories.

Similarly, the groups should provide an inventory of specimens and images available in their repositories for use by investigators in centers, SPOREs and elsewhere. As previously stated, investigators should have access to the system's facilities, including laboratories, regardless of institution.

Correlative laboratory and imaging research (translational research) have been and must remain an essential feature of cooperative group efforts. The groups are the only program within the NCI system that has standardized clinical annotation for large-scale translational research investigations.

The annotated tissue banks and image archives are a resource for the public good that the groups must protect, and which should be made available to non-group scientists. The groups need consistent funding, so as not to separate the tissue banks from the groups' scientific life-blood. For example, the Eastern Cooperative Oncology Group (ECOG) will use tumor characteristics that could be of prognostic and predictive value to stratify patients with stage II colon cancer to identify those patients at increased risk of recurrence.

Each group has database legacy systems that surround

their clinical, imaging, and pathologic material. Because legacy systems have not been created to handle the development of modern therapies, an opportunity exists to imaginatively develop an informatics platform that would interact with centers and SPOREs.

The biostatistical and data management programs of the cooperative groups are based in major cancer centers. Consequently, data integration across the system is critical to engender access to clinical and image data by investigators, independent of their institutional affiliation. The cooperative groups enter approximately 25,000 patients yearly on therapeutic trials and have about 150,000 patients in active follow-up.

As noted above, clinical and image data is intrinsically linked to tissue. The NCI should engage all the biostatistical centers in a dialogue to harmonize cooperative group efforts with their bioinformatics initiatives. A good example is the cancer Biomedical Informatics Grid, whose goal is to help foster data sharing among the components of the system.

The system should take advantage of the cooperative group phase III capabilities that can access large and diverse patient populations, rather than creating new networks or consortia.

As part of the six to nine-month study proposed in the previous section, the group chairs will make recommendations on how the system could be adapted, including how the groups might interact with a national image and bio-specimen network, create a system-wide bioinformatics resource, and develop a preferred approach to pharmacogenetics.

3. Establishing Scientific Priorities. Scientific autonomy has been and will continue to be fundamental to the strength of the entire NCI clinical structure (including the cooperative groups) and to engaging future generations of investigators. This makes establishing scientific priorities especially important. The group chairs believe that the process for setting the scientific agenda could be significantly improved by re-aligning both the intergroup and peer-review mechanisms with the goals of the system.

Many of the incentives built into the intergroup and peer-review systems are counter-productive, leading to the development of more trials than might otherwise be necessary. Today, a group that develops a scientific idea is most likely the only group to receive credit for the resulting trial during the peer-review process.

Consequently, other groups have little incentive to participate in joint or intergroup trials, because they do not receive sufficient recognition. This has created a perverse dynamic in which each group is incentivized to generate ideas and to function as the lead group, but discouraged from participating in trials initiated by other groups.

Priority trials, therefore, are those that are led by each group. The group chairs recommend that the peer-review system be restructured to reward both scientific leadership and participation in group trials.

Traditionally, the group chairs have delegated much of the leadership of the intergroup mechanism to their disease committee leaders. An unintended consequence of this delegation is that the intergroup process has become unaccountable to the groups.

To make the intergroup process more accountable, the group chairs recommend that the Coalition of National Cancer Cooperative Groups oversee the intergroup process and appoint empowered project managers, reporting directly to the Coalition, to design, implement, and coordinate the major intergroup activities.

The proposed structure and process, together with the creation of congruent incentives and recognition for participation in intergroup trials, should result in a tighter focus on the most promising scientific ideas and trials.

As the intergroup and peer-review systems improve, the role of CTEP should change to facilitate the development of studies proposed by the groups, rather than regulate each protocol. CTEP should not control the scientific agenda nor perform its role in a way that would stifle scientific creativity. This proposed change in role should extend through the protocol development and approval processes, as noted in the next section.

The group chairs also recommend establishing national criteria for closing slow-accruing trials. The criteria should trigger discussions in the data monitoring committees about early closure for trials that are not meeting accrual targets. The group chairs are committed to undertaking annual reviews of all open studies and to consider closing studies whose enrollment lags expectation.

4. Accelerating Protocol Development. Activating a group protocol remains a long, laborious, and complex process, involving many steps and multiple layers of review and approval. After the individual group's executive committee has approved the protocol, final system-wide approval can consume an additional 12 to 18 months.

After protocols are released by the groups, they must be approved by CTEP and, now, by the CIRB before submission to the local IRBs. Because all protocols must be reviewed by an institution's IRB, the additional requirement of CIRB review becomes another step in the process, adding six to twelve weeks of delay to the protocol activation process, without contributing meaningfully to trial quality and safety.

And, if new agents are involved, FDA approval is also required and collaboration with industry must be negotiated. As this process has become increasingly inflexible, industry's interest to access the cooperative groups for evaluation of their most promising experimental agents has diminished.

The CIRB was established as a pilot project at 22 institutions (four of which agreed to have the CIRB as the IRB of record). However, before the pilot project was completed, much less evaluated, CIRB review for all phase III studies was required by the NCI. The hasty expansion of the CIRB pilot backfired, because the vast majority of local IRBs do not accept CIRB review as a replacement for their own review.

Although the group chairs support the concept of the CIRB, the group chairs want to see the CIRB validated at the pilot-project level, before it is implemented on a national

scale.

The development cycle of a recently approved CALGB study demonstrates the issues. CALGB protocol 80203 required 17 months to activation, from July 2002 when the CALGB Executive Committee approved it to December 2003. During those 17 months, the concept was sent to CTEP for approval (five-month review); after concept approval the protocol was developed and sent to CTEP for review; comments from CTEP were incorporated, and the protocol was resubmitted to CTEP for approval.

Subsequently, the protocol was sent to the CIRB for comments. The CIRB comments were incorporated, and the amended protocol was sent back to the CIRB for approval. After CIRB approval, the protocol was resubmitted to CTEP for final approval. Because a new agent, cetuximab, is being studied in 80203, the company holding the IND and the FDA also reviewed the protocol.

Delays in protocol activation slow patient accrual. Because completion of pivotal trials depends on speed of protocol development and accrual, needless delays impede the delivery of potentially better therapies from reaching patients. Such delays also discourage industry participation in cooperative group trials at a time when the cooperative groups are trying to build effective public/private partnerships.

The group chairs strongly recommend establishing targets for time to protocol activation and rate of accrual. Within the groups, the group chairs recommend a more interdisciplinary approach that borrows from the best practices from across the groups.

Once the groups release their proposed studies, the CIRB and CTEP roles and review processes should be modified as follows:

1. Eliminate double-review of protocols. CTEP review should only take place when CTEP holds the IND. When a company or group holds the IND, then the FDA alone should review the protocol.

2. When CTEP holds the IND for a registration study, all stakeholders–NCI, cooperative groups, FDA, industry–should collaborate for rapid review and activation.

3. When CTEP review is warranted, CTEP (like the FDA) should be held accountable for providing a timely review. If after 60 days, a group has not heard back from CTEP, the protocol should be deemed approved.

4. Scale back the CIRB to pilot project status, until it has proven that it can reduce the time to protocol activation. In the meantime, eliminate the requirement for CIRB approval before protocol activation.

5. Improving Funding. The Armitage committee report and the implementation committee recommended that the groups be fully funded at the peer-review recommended level. However, the groups remain under funded at approximately 50% of trial costs.

Moreover, funding does not increase as accruals increase, thereby penalizing those groups that exceed their accrual projections. Because the groups' reimbursement levels serve as a contra-incentive to investigators (especially in comparison to industry trials), participation in group trials by researchers is below optimal, which holds back accruals in group trials.

Approximately one-third to one-half of all sites accrue more than ten patients annually. These sites account for 80% to 85% of all accruals. Unless reimbursement levels increase, trying to expand the cadre of physicians who participate in group trials will be futile.

Group investigators and staffs perceive that the system's financial shortfall has worsened, because the demands of the unproven pilot projects and grossly inefficient site visits have diverted scarce resources from their research and increased their workloads.

Unfortunately, group chairs are constrained in their ability to respond, because the funding mechanism, Cooperative Agreements, limits their discretionary authority and control. The group chairs recommend that CTEP facilitate the funding process by providing more flexibility to the group chairs in their interpretation of the Cooperative Agreements.

The group chairs endorse, in the strongest possible terms, the recommendations for full funding called for by the Armitage committee report and the implementation committee. In the meantime, until the overall level of group funding is made proportionate to the cost of the work, the group chairs propose that public/private partnerships be activated to help defray the costs of publicly-funded clinical research.

For example, CRADAs could be used as a funding vehicle to cover the shortfall between the NCI per-case reimbursement and the cost to the site conducting the clinical research.

More importantly, industry trials, whose financial rewards substantially exceed group reimbursement rates, could provide significant support to the system. The group chairs are confident that the groups can facilitate the cancer-drug development approval process for industry. (The groups have been the engine for S-NDAs, and the FDA has accepted the group operating procedures.)

For this to happen, industry-sponsored trials conducted in the cooperative group networks must be recognized in the peer-review process, and accrual to these studies needs to be credited toward the accrual goals for cooperative group sites. As stated in the previous section, industry-sponsored trials should be subject to FDA review only.

Summary of Recommendations

Streamlining the System

1) Harmonize the guidelines for centers, SPOREs, and groups to encourage more cooperation; include patient advocates.

2) Modify the peer-review criteria to encourage collaboration and eliminate disincentives to cooperation among the programs.

3) Remove barriers to participation of investigators, regardless of institutional affiliation.

4) Understand and apply the lessons from the COG merger.

5) Conduct a study to determine the best organizational configuration, workflows, and common data platforms to facilitate data acquisition and sharing across the groups.

6) Document the CTSU's track record. In terms of patient accrual, limit its role to serving as the national enrollment catalyst for rare diseases, minority and underserved populations, and trials of drugs whose patent protection has expired.

7) Enlist patient advocates to improve trial design, access, and adoption of new standards of care.

Adapting the System

1) Use the groups' phase III capabilities (access to large and diverse populations; clinical annotation for translational research). Do not create new networks or consortia.

2) Provide appropriate incentives for centers and SPOREs to function as central laboratories for Group trials.

3) Establish an inventory of available laboratories and their capabilities that all investigators could access.

4) Retain the tissue banks as part of the groups, and adequately fund them.

5) Develop an integrated informatics platform with centers and SPOREs.

Establishing Scientific Priorities

1) Improve the peer-review and intergroup processes to support the system's goals, by rewarding both scientific leadership and cooperation.

2) Appoint the Coalition of National Cancer Cooperative Groups to oversee the intergroup process through empowered project managers reporting directly to the Coalition.

3) Establish national criteria for closing slow-accruing trials; review trials annually.

4) Change the role of CTEP to facilitate, not control, the generation of ideas.

Accelerating Protocol Development

1) Establish targets (timelines and measurements) for protocol development. Success to be measured by time to activation and rate of accrual.

2) Eliminate CTEP review when CTEP does not hold the IND.

3) When CTEP holds the IND for a registration study, all stakeholders should collaborate for rapid review and activation.

4) Establish that CTEP provide timely reviews of ideas and protocols.

5) Scale back the CIRB to pilot status until proven. In the meantime, eliminate the requirement for CIRB approval before protocol activation.

Improving Funding

1) Fully fund the groups.

2) Provide more financial discretion and flexibility to the group chairs.

3) Modify the peer review process (including sites visits) to make it more cost-effective.

4) Promote public/private partnerships to help fund the system. Ensure that the peer-review mechanism and the regulatory process support partnerships with industry.

In Brief:

Emil Frei Wins AACR Award

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of Physicians and Surgeons, where she was chief of the division of medical oncology and director of the Herbert Irving Comprehensive Cancer Center. AACR elected five members to its Board of Directors: **Carlos Arteaga**, Ingram Professor of Cancer Research, Vanderbilt-Ingram Comprehensive Cancer Center; **Stephen Baylin**, professor of oncology and medicine, Sidney Kimmel Comprehensive Cancer at Johns Hopkins University; **Suzanne Cory**, director, Walter & Eliza Hall Institute of Medical Research, Melbourne; **Ronald Levy**, chief, Division of Oncology, Stanford University School of Medicine; and **Carol Prives**; professor of biological sciences, Columbia University. Board members whose terms ended: **Frederick Appelbaum**, Fred Hutchinson Cancer Research Center; **Ronald DePinho**, Dana-Farber Cancer Institute; **Tyler Jacks**, Massachusetts Institute of Technology; **George Vande Woude**, Van Andel Research Institute; and **Barbara Weber**, University of Pennsylvania Cancer Center. . . . **EMIL FREI III** received the first AACR Award for Lifetime Achievement in Cancer Research. Frei is director and physician-in-chief emeritus of the Dana-Farber Cancer Institute, and the first Richard and Susan Smith Distinguished Professor of Medicine at Harvard Medical School. With **Emil Freireich**, he developed the first treatment leading to a complete cure for childhood leukemia. Working with **James Holland**, Frei and Freireich developed the treatment approach of combination chemotherapy. "Specialists regard combination chemotherapy as the single most important advance in cancer treatment in the last quarter-century," said Karen Antman, AACR past president. "In cases of childhood leukemia alone, the cure rate has risen from zero in 1955 to 80 percent today, thanks to Dr. Frei's innovative method." . . . . **WILLIAM HAIT** was appointed to a five-year term as editor-in chief of the AACR journal Clinical Cancer Research. He succeeds **John Mendelsohn**, president of M.D. Anderson Cancer Center. Hait is director of The Cancer Center of New Jersey. . . . **AACR 50-YEAR MEMBERS** were recognized at the annual meeting: **Mary Argus**, **Renato Baserga**, **Joseph Greenberg** (deceased earlier this year), **Hilary Koprowski**, **Paul Kotin**, **Edwin Mirand**, **Edward Modest**, **George Moore**, **Charles Nichol**, **Agnes Stroud-Lee**, **Arthur Upton**, and **Jane Wright**.

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